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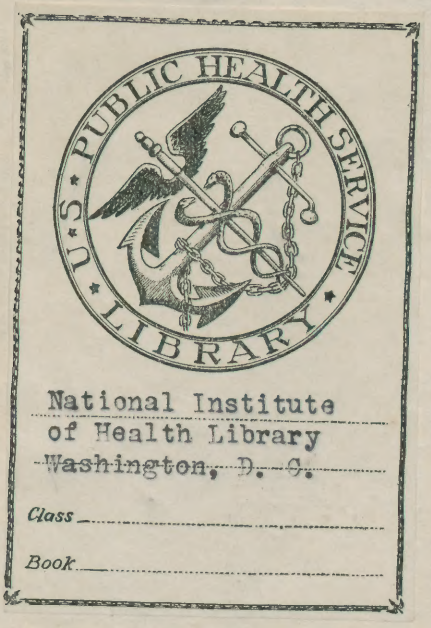

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NON-DISJUNCTION AS PROOF OF THE CHROMOSOME THEORY OF HEREDITY

CALVIN B. BRIDGES
Columbia University, New York City

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NON-DISJUNCTION AS PROOF OF THE CHROMOSOME THEORY OF HEREDITY[1]

CALVIN B. BRIDGES
Columbia University, New York City

[Received October 21, 1915]

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I

INTRODUCTION

There has been a long series of observations and experiments which has led more and more definitely to the conclusion that the chromosomes are the bearers of the hereditary materials.[2] It was observed that male and female contribute equally to the inheritance of the offspring, and yet the contribution of the male consists of little more than a nucleus. That

[1] Contribution from the Zoological Laboratory of Columbia University.

[2] For a fuller discussion of the steps in the accumulation of this evidence see "The mechanism of Mendelian heredity" by MORGAN, STURTEVANT, MULLER, and BRIDGES.

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inheritance is a function of the nucleus rather than of the cytoplasm is shown by many embryological and cytological facts. Attention was next narrowed to the chromatin and chromosomes. Embryological experiments showed that the chromosomes are qualitatively different and that a full complement is essential to normal development. The increasing cytological knowledge of mitotic division and of gametogenesis made it clear that the chromosomes were qualified to serve as the material basis of heredity.

The next advance was the result of the exact knowledge of heredity which Mendelian analysis furnished, and of the coupling of experimental genetics with cytological investigation. It was shown that the genes for characters and the chromosomes have the same *method* of distribution. More recently cases have arisen in which genes and chromosomes have the *same* distribution. The final step has been to demonstrate the *identity of distribution between specific genes and specific chromosomes* in such a way that the argument of "the-cell-as-a-whole" cannot be applied, and in such a way that the chromosomes must be regarded as the means and not the consequence of the inheritance of characters and of sex. The experimental and cytological evidence in the case of non-disjunction furnishes such a demonstration.

An account of the discovery of non-disjunction and of its effect upon sex-linked inheritance was published (BRIDGES 1913 b) in the JOURNAL OF EXPERIMENTAL ZOOLOGY for November 1913. A further account in the form of a summary was given in SCIENCE, July 17, 1914 (BRIDGES 1914).

The work on non-disjunction started from exceptions in certain experiments which I was carrying out with Prof. T. H. MORGAN (MORGAN and BRIDGES 1913). The work was continued while I was assisting Dr. MORGAN, and my most sincere thanks are due for the opportunity and the encouragement which he offered. The frequent consultations and the constant association with Dr. A. H. STURTEVANT, Dr. H. J. MULLER, and other workers in the laboratory have brought out possibilities that would otherwise have been overlooked.

A brief statement concerning sex determination, normal sex-linked inheritance, etc., which form the background of these experiments may first be made.

THE SEX CHROMOSOMES AND SEX

The female of *Drosophila ampelophila* has a pair of sex chromosomes (X chromosomes) and three pairs of autosomes. The medium sized

straight chromosomes shown by the diagram to the left in figure 1 are identified as the pair of X chromosomes.

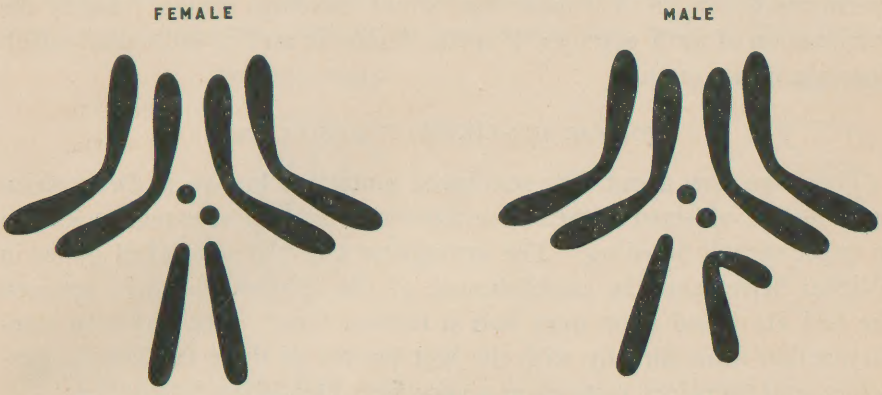


FIGURE 1.—Diagram showing the characteristic pairing, size relations, and shapes of the chromosomes of *Drosophila ampelophila*. In the male an X and a Y chromosome correspond to the X pair of the female. The relative lengths of the chromosomes of this diagram are based upon averages of the measurements of the figures in plate 1; on the basis of X = 100 the length of each long autosome is 159, of each small autosome 12, of the whole Y 112, of the long arm of the Y 71, and of the short arm 41.

The chromosomes of the male have presented serious difficulties in spite of the very great amount of study devoted to them. Miss STEVENS (1908 a) made a prolonged study involving the dissection and examination of some two thousand individuals. She described the three pairs of autosomes of the male as the same as those in the female, and the sex chromosomes as *"a clearly unequal pair"*.[3] The cytological work which I have done on males and on females having an extra Y shows that X is somewhat shorter than Y, that it is typically straight, and attached to the spindle fiber by its end. On the other hand, the Y chromosome (see figure 1 to the right) is somewhat longer than the X, is attached not by its end, but sub-terminally, and typically has the shape of a J or of a V with one of the arms shorter than the other. Drosophila is therefore a member of the group of forms in which the male produces two kinds of sperm, half with an X and half with a Y chromosome. All

[3] Miss STEVENS supposed the longer of these two chromosomes to be the chromosome present in duplex in the female, and that a distinct "X" piece constituted the middle of this long heterochromosome, so that at the time at which the first paper on non-disjunction was written (BRIDGES 1913 b), it had become the general belief that the constitution of the male was XO and of the female XX. The X chromosome was supposed to be attached to an autosome, as in Ascaris.

the eggs of the female are alike, each carrying an X after the polar bodies have been given off. The fertilization of an X egg by an X sperm results in an XX individual which develops into a female; the fertilization of an X egg by a Y sperm results in an XY individual which develops into a male.

NORMAL SEX-LINKED INHERITANCE

There are now about fifty sex-linked mutations known in Drosophila, and the data collected in their investigation are the most extensive known in experimental breeding. The arrangement of the sex-linked genes in a linear series and the establishment of the relative distances between the loci are based upon over half a million flies.[4] The work on non-disjunction deals directly with the best known of these sex-linked characters, and therefore rests upon a very firm Mendelian foundation.

The inheritance of a recessive sex-linked character may be illustrated by the cross of a vermilion female by a wild type (red-eyed) male (see figure 2). The sons are vermilion-eyed like the mother, and the daughters are wild type like the father. This criss-cross inheritance is explained by the theory that the genes for the sex-linked characters are carried by the X chromosomes. As shown in figure 2, the son derives his single X chromosome from his mother, and shows vermilion eye color because the gene for vermilion was carried by that chromosome. The Y chromosome from the father does not affect the visible characters of the son in any way. Thus a male always shows by its characters what genes are carried by its X chromosome. The daughter receives from the mother an X carrying the vermilion gene, but since the vermilion is recessive to the unmutated gene (red) carried by the X which she receives from the father, she will be wild type (red).

THE CHARACTERS USED AND THEIR LINKAGE RELATIONS

When vermilion is crossed to sable (a sex-linked recessive body-color) there are more vermilion grandsons and sable grandsons than grandsons that are both vermilion and sable or neither (i.e. wild type). If the gene for vermilion was carried by the maternal X and the gene for sable by the paternal X, the vermilion sable and wild type grandsons must have been produced through a process which may be called crossing over. The simplest way in which this crossing over may be assumed to take place

[4] Carnegie publication No. 237 by MORGAN and BRIDGES gives the most recent account of the sex-linked characters and of the linkage data which had been obtained prior to June 1914.

is shown in figure 3. The two X chromosomes come together and twist about each other, with homologous regions of the two chromosomes lying side by side. The genetic evidence requires that the chromosomes break across and then reunite in such a way that each of the chromo-

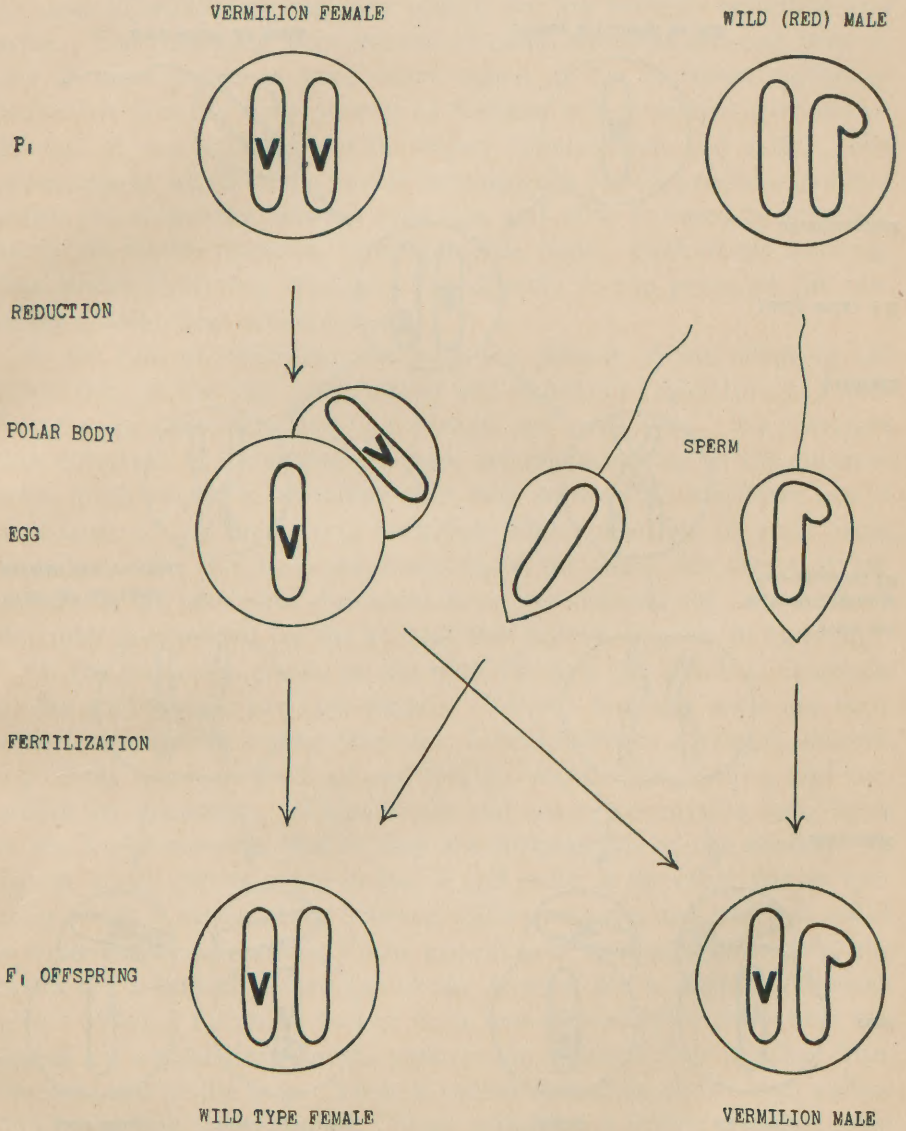


FIGURE 2.—The relations of the sex chromosomes to sex production and to the inheritance of the sex-linked character vermilion eye-color. The X chromosomes are represented as straight rods and the Y as J-shaped. The females with v in only one of the two X's do not show the recessive vermilion character.

somes is composed of an original piece joined to the succeeding piece of its mate. Crossing over may be supposed to occur at any point along the chromosome. The right side of the diagram of figure 3 illustrates such a crossing over occurring between the loci for vermilion and sable.

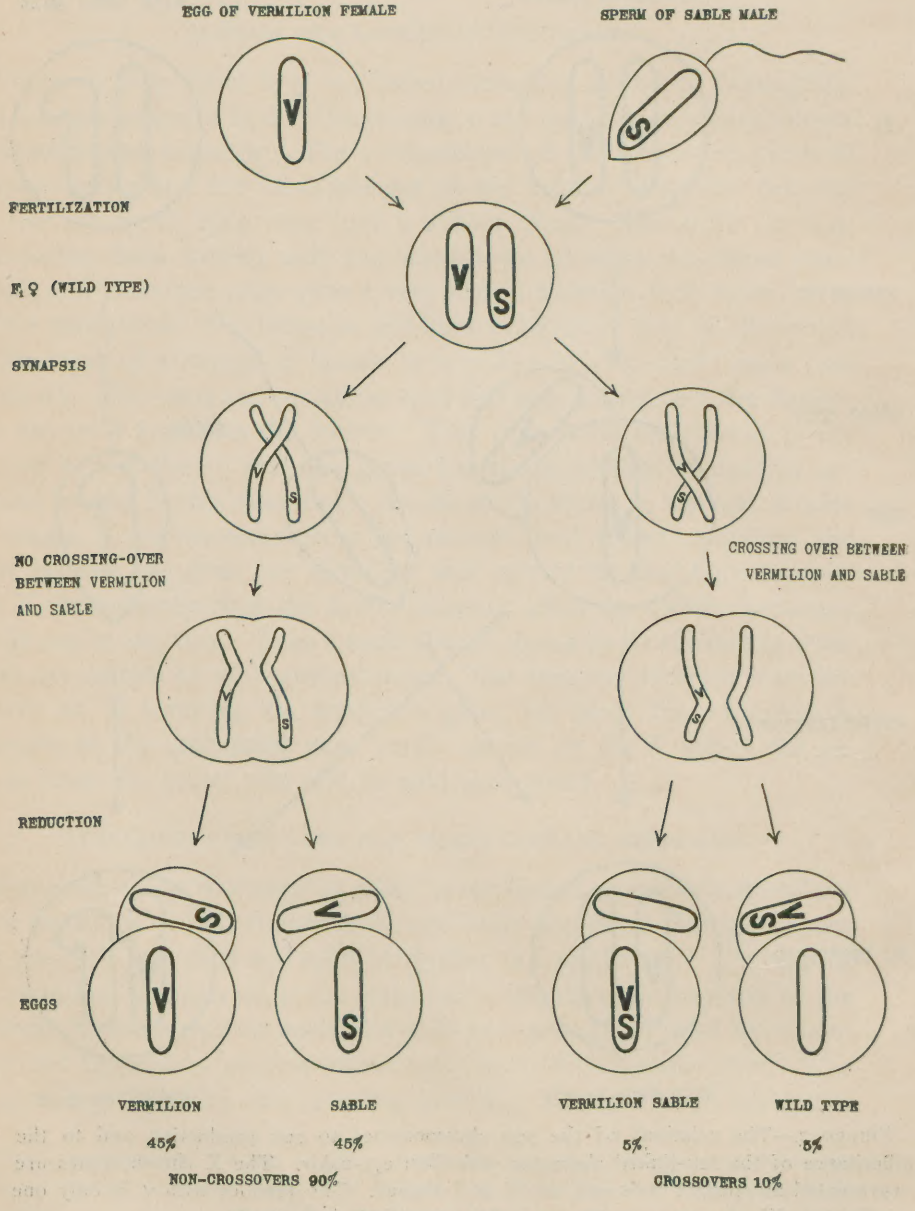


FIGURE 3.—Diagram to show crossing over.

Only ten percent of all the offspring are found to have resulted from crossing over between vermilion and sable. It is known from certain experiments that in about forty percent of cases there is no crossing over whatever between the two X chromosomes. Of the sixty percent of cases in which crossing over occurs, ten are between vermilion and sable. The remaining fifty percent of cases represent crossing over at one or more points in some other region of the X; these ineffective crossovers plus the forty percent of absolute non-crossovers give ninety percent of non-crossovers with respect to vermilion and sable. The percentage in which such a doubly heterozygous female produces gametes which are crossovers between vermilion and sable is tested by breeding her to the double recessive, vermilion sable, male. Each of the resulting flies shows characters corresponding directly to the genes of the maternal gamete from which it came.

In the case of vermilion and sable ten percent of the offspring are crossovers; in the case of vermilion and miniature (miniature is a sex-linked wing-character) only 3.1 percent are crossovers. We interpret this difference to mean that the gene for miniature lies in the chromosome much nearer to vermilion than does sable—that miniature lies at a distance of 3.1 units from vermilion while sable lies 10 units from vermilion. On this basis the positions of the genes for the most important of the sex-linked characters have been mapped out. As much of this map as is needed for the account that follows is given in figure 4.

Of the characters shown on the map, the only one which is dominant to the wild type is bar (eye-shape). Yellow, tan, and sable are body colors; miniature is a wing-character; forked refers to a scraggly branching of the spines of the head and thorax; white, eosin, cherry, and vermilion are eye-colors. White, eosin, and cherry occupy the same locus in the X chromosome, that is, they are allelomorphs of one another. A female which carries white in one X and eosin in the other has an eye-color which is intermediate between white and eosin and which is called a white-eosin compound. Eosin eye-color is markedly dimorphic, the males are a pinkish yellow, while the females are a slightly yellowish pink. When a fly shows two or more non-allelomorphic characters, the names are written from left to right in the order of their position from the zero end of the map. Thus, a yellow forked fly shows both yellow body-color and forked spines. Eosin vermilion, a double recessive form in which both characters are effects upon the eye-color, is a pale cream color (darker in the female than in the male) very easily separated from both eosin and vermilion.

The system of symbols used in the diagrams and table headings is as follows. The gene for a recessive mutant character is represented by a lower-case letter, as t for tan and v for vermilion. The symbols for eosin and cherry, which are allelomorphs of white, are w^e and w^c. The symbol for the dominant mutant character, bar, is B′. The symbols for the allelomorphs of the mutant genes are the converse letters, as b′(not-bar), but are now usually omitted. The same letters that are used to

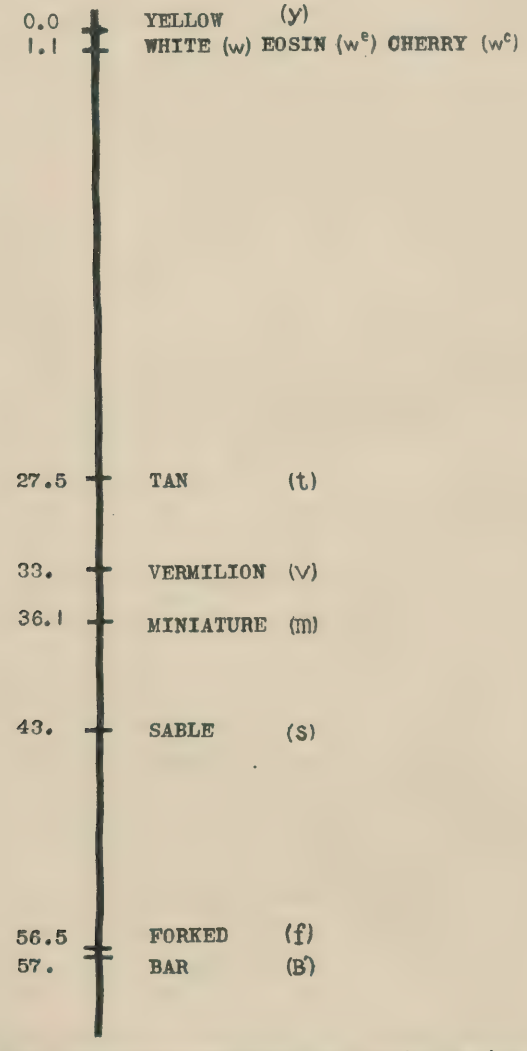


FIGURE 4.—Map of the linear arrangement and relative spacing of the genes for sex-linked characters. The letters, used both as the symbols for the genes and as abbreviations of the names of the characters, are included in parentheses.

represent the genes are also used as symbols of the names of the somatic characters shown by the flies. The symbol + is read "wild type" and indicates that the flies classified under this heading show no mutant characters.

PRIMARY NON-DISJUNCTION IN THE FEMALE

Ordinarily, as in diagram 2, in a cross to a male with the dominant character all the sons and none of the daughters show the recessive sex-linked characters of the mother. Similarly, all the daughters and none of the sons show the dominant sex-linked characters of the father. The peculiarity of non-disjunction is that sometimes a female transcends these rules and produces a daughter like herself (a matroclinous daughter) or a son like the father (a patroclinous son), while the rest of the offspring are perfectly regular, showing the expected criss-cross inheritance. Such exceptions, produced by a normal XX female, may be called primary.

The production of primary exceptions by a normal XX female may be supposed to result from an aberrant reduction division at which *the two X chromosomes fail to disjoin from each other. In consequence both remain in the egg or both pass out into the polar body.* In the former case the egg will be left with two X chromosomes and in the latter case with no X.

If the genes for sex-linked characters are carried by the X chromosomes, then each of the X chromosomes of the XX egg of a vermilion female will carry the gene for vermilion. The fertilization of such XX and zero eggs by the X and by the Y spermatozoa of a wild male will result in four new types of zygotes, as shown in figure 5.

(1) The XX egg fertilized by the X sperm gives an XXX zygote which might be expected to develop into a female. No females of this class have been found, and it is certain that they die.

(2) The fertilization of the XX egg by the Y sperm gives rise to a female having an extra Y chromosome (XXY). Since both of the X chromosomes came from the vermilion-eyed mother, this daughter must be a vermilion *matroclinous exception.*

(3) The fertilization of the zero egg by the X sperm gives rise to a male which has no Y chromosome (XO), and whose X coming from his red-eyed father brings in the red gene which makes the son a *patroclinous exception.* These XO males are viable but are completely sterile.

(4) The zero egg by the Y sperm gives a zygote (OY) which is not viable.

Perhaps the cause of the initial aberrant reduction which constitutes primary non-disjunction is a mechanical entanglement (an incomplete untwisting from a strepsinema stage) of the two X chromosomes, resulting in a delayed reduction. In such cases the formation of the cell boundaries would catch the lagging X's and include them in one or the other cell, and perhaps very often (as in certain nematodes) would pre-

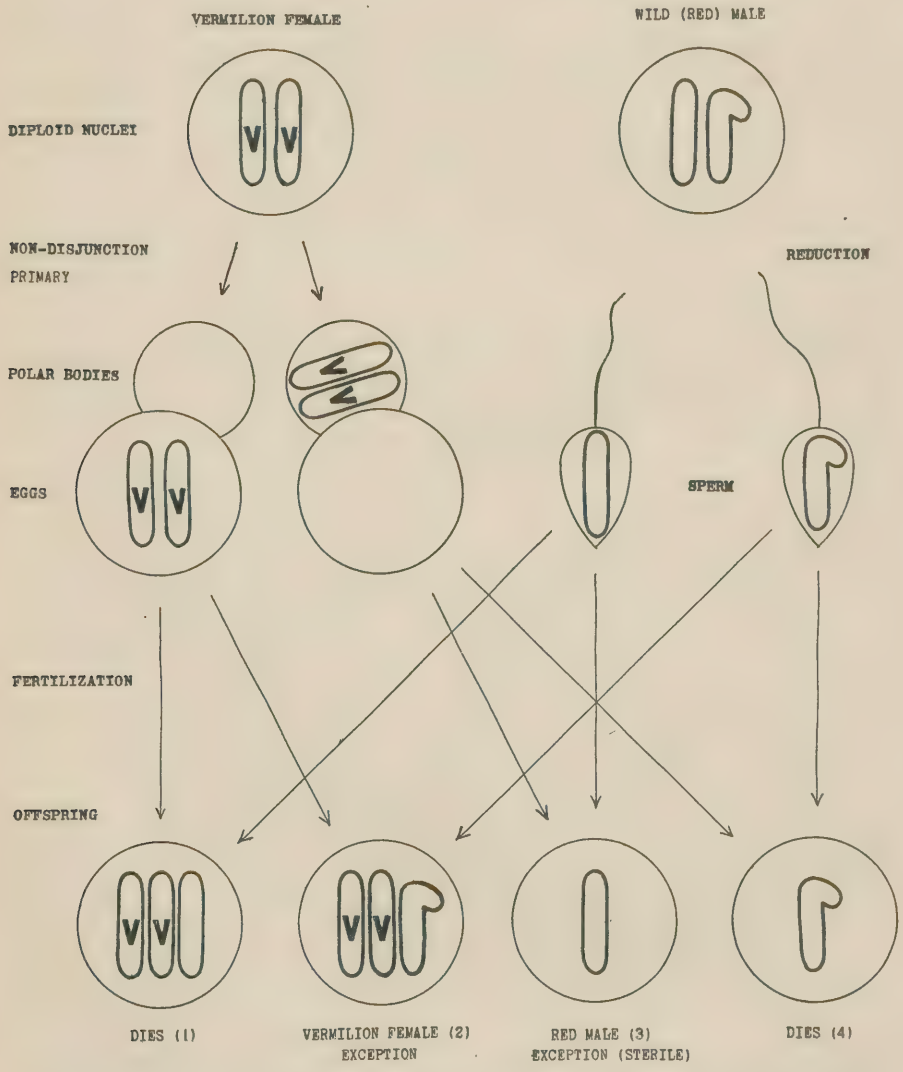


FIGURE 5.—Diagram of the production by a vermilion-eyed female of XX and zero eggs through *primary* non-disjunction, and the progeny resulting from the fertilization of such eggs by the sperm of a red-eyed male.

vent their leaving the middle of the spindle to join either daughter nucleus. If such an occurrence were common there should be more zero than XX eggs and consequently more primary exceptions should be males than females.

In studying primary non-disjunction we are dependent on what material chance offers, since we know of no means of controlling the process. It is equally as likely that an egg produced by primary non-disjunction will become a non-viable zygote (XXX and OY) as that it shall be viable (XXY and XO). For this reason it is impossible to detect half of those cases of primary non-disjunction which really occur. The XO male is viable and should offer an interesting field for further work, but—he is sterile. The direct opening offered for further work is through the matroclinous XXY daughter, which is perfectly fertile and which produces further exceptions which we may call secondary.

PRIMARY NON-DISJUNCTION IN THE MALE

If primary non-disjunction occurred in the male, XY and zero sperm would be formed, but the zygotes from them would not differ in their sex-linked characters from regular offspring, so that such an occurrence could not be detected immediately. However, the XY sperm would give rise to XXY daughters, and these in turn would produce secondary exceptions which could be observed.

Primary non-disjunction has been actually seen to occur in the male of Metapodius. WILSON found three spermatocytes in which X followed Y to one pole at the reduction division (WILSON 1909).

SECONDARY NON-DISJUNCTION IN THE FEMALE

It has been shown that matroclinous daughters of the constitution XXY may arise as the result of primary non-disjunction. The results from the outcrossing of several matroclinous daughters to males having other sex-linked characters were given in 1913. Of unusual interest was the appearance in F_1 of about four[5] percent of further exceptions (secondary exceptions). That is, about four percent of the daughters were like the mother and four percent of the sons were like the father. The remaining sons and daughters were of the kinds expected.

The explanation given at first for the fact that exceptional daughters inherit from their mother the power of producing exceptions, was that each X of the exceptional female carried a gene which caused these

[5] In previous papers the percentage of exceptions has been given roughly as five. The mean of all data now on hand is 4.3 percent of exceptions (see page 16).

chromosomes to undergo reduction abnormally in a small percentage of cases. Since these chromosomes descend directly to their exceptional daughters, they would transmit to those daughters the same gene and consequently the same power of producing exceptions.

Later work has provided data which can not be explained by appealing to the action of a gene in the X chromosome, and which prove that these secondary exceptions are due to the presence of the extra Y. In an XXY female there are three homologous sex chromosomes, between any two of which synapsis may occur, that is, synapsis may be of the XX or the XY type (homo- and heterosynapsis). In only about sixteen percent of cases (see page 17) does heterosynapsis occur, while about 84 percent of cases are homosynaptic and the Y remains unsynapsed. At the reduction division the two chromosomes that have synapsed, disjoin, one going to each pole, and the free chromosome goes to one pole as often with the one as with the other of the disjoined chromosomes. Thus, after heterosynapsis the reduction divisions are of two kinds, the XX-Y and the X-XY types. Half the eggs that come from the XX-Y type of reduction are XX and the other half are Y. For the X-XY type the eggs are X and XY, as many of one kind as of the other. After homosynapsis all the reductions are X-XY. As a result of reduction of these two types there are four classes of eggs—two of which, X and XY, are composite and large (46 percent), and two of which, XX and Y are of single origin and small (4 percent). If these eggs are produced by a vermilion-eyed female, both of whose X chromosomes carry the recessive gene for vermilion, then the eight classes of zygotes shown in figure 6 will result upon fertilization by a wild male, which produces X and Y sperm.

The XX eggs fertilized by X sperm give XXX individuals (figure 6, 1) which are unable to live.

The XX eggs fertilized by the Y sperm give individuals (5) which are exact duplicates of their mother in their sex chromosomes, and like her are females each containing an extra Y chromosome. Since the gene for vermilion is carried by the X chromosome, these females have vermilion eyes and hence are matroclinous exceptions. Since they have not received an X from their father, they can neither show nor transmit his sex-linked characters. If in the mother the presence of the extra Y led to the production of secondary exceptions, then these XXY daughters should also give exceptions, and this is in fact the case.

The Y eggs fertilized by the X sperm give males (2). These males have received their X from their father and they show his sex-linked

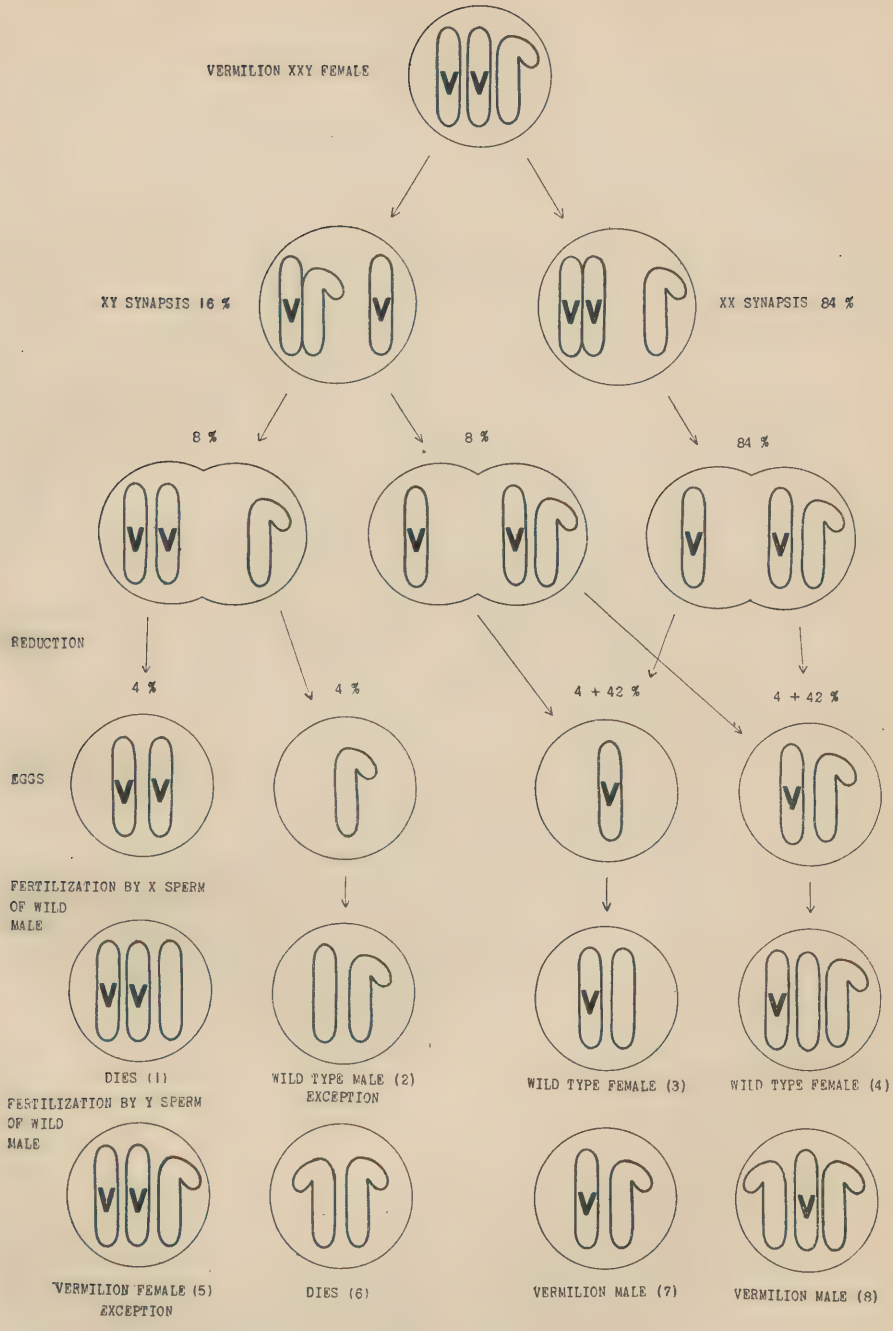


FIGURE 6.—Secondary non-disjunction in the female. Diagram showing the constitution of an exceptional vermilion female, the two types of synapsis, reduction, and the four classes of eggs produced. Each kind of egg may be fertilized by either of the two (X and Y) kinds of sperm of the wild male, giving the eight classes of zygotes shown.

characters, that is, they are patroclinous exceptions. Since in chromosome constitution (XY) these males are not different from ordinary males, they should have no power of producing exceptions. This has been shown to be the case.

The Y eggs fertilized by Y sperm give YY individuals (6) which are unable to live.

The X eggs by X sperm give regular XX females (3), and by Y sperm give regular XY males (7). Neither of these two classes is able to produce secondary exceptions or to transmit non-disjunction.

The XY eggs by X sperm give XXY females (4) *which, because of the extra Y, possess the power of producing secondary exceptions, though they themselves are not exceptions.*

The XY eggs by Y sperm give XYY males (8). These males do not give rise to genetic exceptions in F_1, but they endow some of their daughters with an extra Y (XY sperm and X egg) which enables these daughters to produce secondary exceptions.

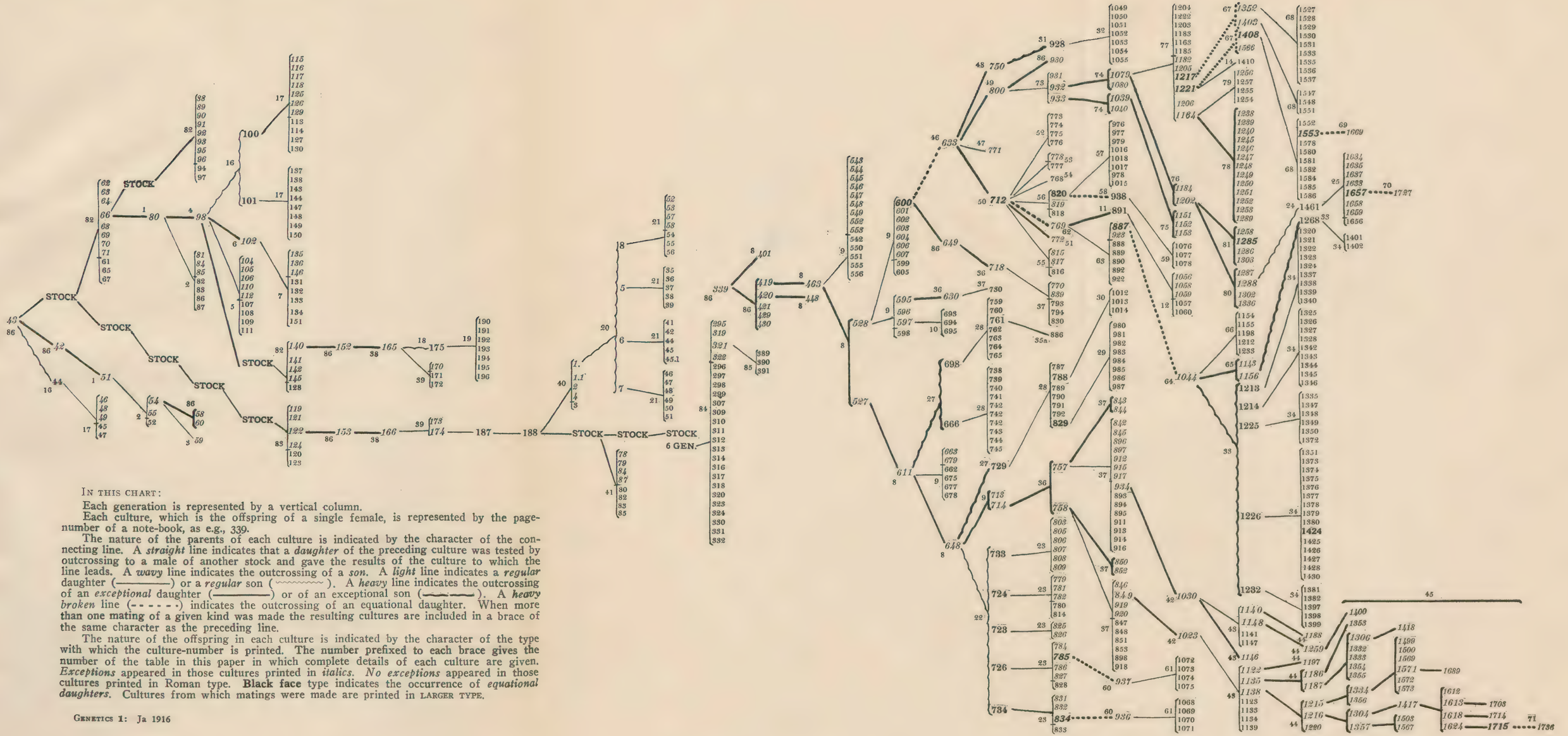
By breeding in each generation the exceptional daughters with the exceptional sons a line was maintained in which the entire set of sex-linked genes of the mother was handed down to the exceptional daughters and the entire set of the father to the exceptional sons.

That the XX eggs which developed into matroclinous exceptions had really been fertilized by normal sperm of the father was proved by the introduction into such daughters of autosomal genes from the father. The inheritance was uniparental with respect to the sex-linked genes, but biparental and wholly normal with respect to the autosomal genes. The fact that exceptional offspring inherit sex-linked characters from only one parent, but at the same time inherit the autosomal characters from both parents is explained if the sex chromosomes are the only chromosomes which have undergone non-disjunction, the ordinary chromosomes disjoining normally.

II

NEW DATA

All the facts presented in the first paper on non-disjunction can be explained, as has just been shown, on the assumption that the genes for sex-linked characters are carried by the X chromosomes and that these X chromosomes sometimes fail to disjoin, either primarily, or because of the presence of an extra Y (secondary non-disjunction). The new data now presented furnish evidence upon several other points suggested by



IN THIS CHART:

Each generation is represented by a vertical column.

Each culture, which is the offspring of a single female, is represented by the page-number of a note-book, as e.g., 339.

The nature of the parents of each culture is indicated by the character of the connecting line. A *straight* line indicates that a *daughter* of the preceding culture was tested by outcrossing to a male of another stock and gave the results of the culture to which the line leads. A *wavy* line indicates the outcrossing of a *son*. A *light* line indicates a *regular* daughter (————) or a *regular* son (〰〰〰). A *heavy* line indicates the outcrossing of an *exceptional* daughter (————) or of an exceptional son (— — —). A *heavy broken* line (- - - - -) indicates the outcrossing of an equational daughter. When more than one mating of a given kind was made the resulting cultures are included in a brace of the same character as the preceding line.

The nature of the offspring in each culture is indicated by the character of the type with which the culture-number is printed. **The number prefixed to each brace gives the** number of the table in this paper in which complete details of each culture are given. *Exceptions* appeared in those cultures printed in *italics*. *No exceptions* appeared in those cultures printed in Roman type. **Black face** type indicates the occurrence of *equational daughters*. Cultures from which matings were made are printed in LARGER TYPE.

the hypothesis, and also upon many points which the simple analysis failed to reveal.

The value of the evidence upon the main points has been increased by repeating a given test at different times and with different stocks or lines. Likewise the same test was often paralleled by starting more than one set of parents and then keeping separate the results from each. The tests have been further checked by using many different combinations of the most workable of the sex-linked characters. This method of distributing the tests over a great variety of material imparts to the conclusions a generality which they might not otherwise possess. One test in most of the sets is carried out much more extensively than the others in order to know fully the results given by some one individual of a given type.

It would be impossible to be brief and yet make entirely clear by text and table headings the relations between the parts of an experiment, when these parts are similar in nature but different in origin. Accordingly, reference may be made with advantage to the pedigree opposite page 14, which includes all the cultures considered in this paper.

THE PERCENTAGE OF SECONDARY EXCEPTIONS

In the first paper on non-disjunction (BRIDGES 1913 b) the results of about twenty-five cultures which gave secondary exceptions, gave the following totals:

TABLE I

A summary of the offspring of XXY females from BRIDGES *1913 b.*

Regular offspring		Exceptions		Total	Percent of exceptions
Daughters	Sons	Daughters	Sons		
2,929	2,677	133	158	5,877	4.6

The various secondary cultures reported in this paper bring these totals up to:

TABLE II

Total of secondary exceptions from BRIDGES *1913 b and this paper.*[6]

Regular offspring		Exceptions		Total	Percent of exceptions
Daughters	Sons	Daughters	Sons		
27,679	26,391	1,235	1,169	56,474	4.3

[6] These data are from tables 1-9, 11, 12, 17, 23, 25, 35a, 37, 38, 40, 41, 43-46, 48-51, 53, 55, 58, 60, 62-65, 67-71, 73-75, 78, 80-84, 86. The cultures known to be high non-disjunction are omitted.

In addition to these cultures there are several cultures in which the exceptional daughters could not be separated from the regular daughters, but in which the sons could be classified as regular and exceptional. The total of such cultures give:

TABLE III

Additional secondary cultures in which the sons only are separable.[1]

All daughters	Regular sons	Exceptional sons	Total sons	Percent of exceptions
1,681	1,496	77	1,573	4.3

The value given by these sons alone is the same as that given by the former cultures, namely, 4.3.

THE EQUALITY OF THE EXCEPTIONAL SONS AND DAUGHTERS OF XXY FEMALES

The total of the sons in tables II and III, is 29,133 of which 1,146 or 4.3 percent were exceptions. The daughters of table II total 28,914 of which 1,235 or 4.3 percent were exceptions. It is evident that the percent of exceptional daughters is the same as the percent of exceptional sons. This equality goes back to and proves an equality of XX and Y eggs (see figure 6, p. 13). These eggs are produced after XY synapsis when X and Y disjoin and the free X goes with the disjoined X, that is, by the XX-Y type of reduction. The XX eggs are produced when the Y goes to the polar body, and the Y eggs when both X's go to the polar body. Since it has been shown that there are as many XX as Y eggs it must be a matter of chance whether any particular egg receives the XX or the Y end of the spindle. In another section it will be shown that also in the other type of reduction, namely, the X-XY type, the free chromosome goes to the polar cell as often as it remains in the egg, so that the number of XY eggs is equal to the number of X eggs. Although there is no evidence that reductions are not taking place at random, there is proof that the synapses in an XXY female are strongly preferential, homosynapsis occurring much oftener than is expected on chance.

THE RELATION BETWEEN THE PERCENT OF HETEROSYNAPSIS AND THE PERCENT OF SECONDARY EXCEPTIONS

By reference to figure 6, page 13, it will be seen that the exceptional offspring are derived from germ-cells in which XY synapsis had

[1] These data are from tables 21, 36, 39, 42, 47, 79.

occurred. Not all the germ-cells in which heterosynapsis occurred lead to the production of exceptions, but there is a definite relation such that the percent of exceptions which should follow from a given percent of heterosynapsis can be calculated; and, vice versa, from the observed percent of exceptions the percent of cases of XY synapsis necessary to give rise to these exceptions can be determined. Let us assume that in an XXY female sixteen percent of all synapses are between Y and one or the other of the two X's. At reduction the Y and the X disjoin, and the free X goes to the same pole with X as often as with Y, so that in eight percent of cases the reduction is of the XX-Y type. After XX-Y reductions there are four percent of XX and four percent of Y eggs. Half of these eggs are fertilized by X and the other half by Y sperm, so that the zygotes are XXX, XXY, XY, and YY, each class comprising two percent of the whole number of zygotes. The XXX and YY zygotes die, while the XXY and XY zygotes give rise to exceptions, that is, $\frac{4 \times 100}{96}$ or 4.2 should be the percent of exceptions surviving after sixteen percent of XY synapses. The percent of exceptions calculated from all the data is 4.3 which corresponds to 16.5 percent of heterosynapsis. This value was calculated by means of the formula $x = \frac{400\,y}{100 + y}$ in which x represents the percent of heterosynapsis and y represents the corresponding percent of exceptions. The converse formula $y = \frac{100\,x}{400 - x}$ is also useful. Curve *a* of figure 7 on page 18 gives for every percent of XY synapsis the corresponding percent of exceptions which should be observed. If all the synapses are between Y and one or the other X, then the percent of exceptions should be the upper limit of 33.3.

THE COEFFICIENT OF Y SYNAPSIS

If the synapses in an XXY female take place according to chance there should be twice as many XY as XX synapses. In order that the synapses have this distribution the three sex chromosomes must be equally potent in synapsis, that is, the synapsis coefficient of a Y in terms of an X must be 100 percent. With a synapsis coefficient of 100, 66.7 percent of the synapses should be between Y and an X, and there should result twenty percent of exceptions. Ordinarily not twenty but 4.3 percent of exceptions are produced, and the coefficient of Y must accordingly be far below 100. The relation between the coefficient of Y (c) and the percent of heterosynapsis (x) is expressed by the formulae $c = \frac{50\,x}{100 - x}$ and $x = \frac{100\,c}{50 + c}$.

In a previous section we found that the percent of heterosynapsis (x) was 16.5 so that the formula $c = \frac{50\,x}{100 - x}$ enables us to calculate the normal coefficient of Y as 9.9.

THE RELATION BETWEEN THE COEFFICIENT OF Y AND THE PERCENT OF EXCEPTIONS

Ordinarily the relation which is most useful is not that between the coefficient of Y and the percent of heterosynapsis but that between the coefficient of Y (c) and the percent of exceptions (y). By substituting the value for x just found, namely, $\frac{100\,c}{50 + c}$, for x in the formula $y = \frac{100\,x}{400 - x}$, y is found to be equal to $\frac{100\,c}{200 + 3\,c}$, and $c = \frac{200\,y}{100 - 3\,y}$. Curve *b* figure 7 gives graphically the relation between the coefficients of Y (up to 100) and the percents of exceptions.

A knowledge of the value of x, y, or c enables the other two values to be calculated from the two curves *a* and *b* or by the six formulae given.

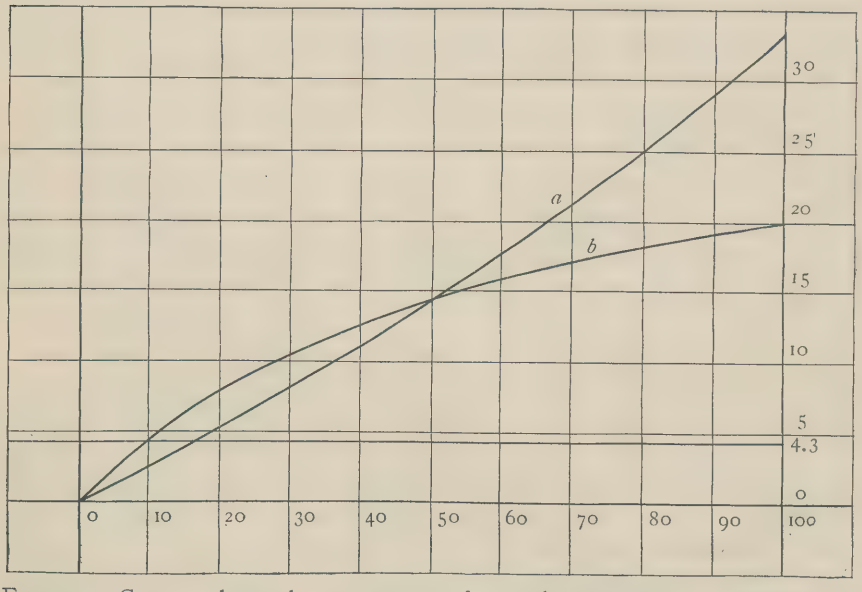


FIGURE 7.—Curve *a* shows the percentages of secondary exceptions (ordinates) corresponding to various percentages of XY synapsis (abscissas).

Curve *b* shows the percentages of exceptions (ordinates) corresponding to various coefficients of Y (abscissas). The line at 4.3 indicates the mean percent of observed secondary exceptions. This line intersects curve *a* at 16.5 and curve *b* at 9.9.

THE EQUALITY OF XXY AND XX FEMALES AMONG THE REGULAR DAUGHTERS OF XXY FEMALES

Figure 6 shows that the regular daughters, although all alike externally, must be supposed to be of two classes with respect to their sex chromosomes. One class (fig. 6, (3)) is XX and the other (4) is XXY. If the presence of the extra Y causes secondary exceptions to occur, then these XXY daughters should produce exceptions even though they themselves were not exceptions. If in reductions of the X-XY type, the X and the XY group remain in the eggs equally often, then these XX and XXY daughters should be in equal numbers, that is, half of the regular daughters should produce exceptions. That this is the case is shown by the experiments which follow.

The first regular daughters tested were those obtained by crossing two eosin exceptional females to wild males.

TABLE 1

The offspring given by two eosin exceptional females when outcrossed by two wild males.

No.	Regular Offspring		Exceptions		Percent of exceptions
	+♀	w^e♂	w^e♀	+♂	
51n	105	119	6	10	6.7
80n	83	93	6	4	5.4
Total	188	212	12	14	

Eosin is recessive, so that the regular daughters which are heterozygous for eosin do not differ in appearance from wild flies. These daughters must be tested by males which have some sex-linked character different from those already in the cross, otherwise we could not distinguish between the patroclinous exceptions and the regular sons. White bar males, which differ in two characters from any regular son, were used in testing these females.

The exceptional sons produced were white bar, and the exceptional daughters did not receive the dominant bar from the father and were accordingly wild type. The females tested proved to be of two sorts: five gave exceptions and five did not give exceptions. These females must have been of the types XXY and XX as anticipated.

One of the regular white-eosin bar daughters of culture 54n seemed to have a darker eye-color than her sisters. When she was bred to a

TABLE 2

The two kinds of results given by the regular daughters from table 1 when tested by white bar males.

No.	Regular daughters		Regular sons		Exceptions		Percent of exceptions
	w-w^e B′	B′	w^e	+	+♀	w B′♂	
54n	90	92	111	101	11	13	5.7
55n	17	26	17	21	—	1	1.2
81n	50	54	44	65	2	2	1.9
84n	31	34	27	33	1	1	1.6
85n	38	46	30	43	1	3	2.5
Total	226	252	229	263	15	20	3.5
52n	116	124	110	121	—	—	—
82n	40	43	28	32	—	—	—
83n	85	47	63	57	—	—	—
86n	54	57	53	45	—	—	—
87n	21	23	26	13	—	—	—
Total	316	294	280	268	—	—	—

wild male she gave only the expected eye-colors. This regular daughter proved to be XXY and the percentage of non-disjunction which she gave was unusually high.

TABLE 3

The offspring given by a regular w-w^{e}B′ daughter from culture 54n when tested by a wild male.

No.	Regular daughters		Regular sons				Exceptions		Percent of exceptions
			$\frac{w \quad B'}{w^e}$		$\frac{w}{w^e \mid B'}$				
	+	B′	wB′	w^e	w	w^{e}B′	w-w^{e}B′♀	+♂	
59n	28	34	26	18	13	13	11	12	14.8

The regular sons of table 3 show the amount of crossing over between white and bar. The original or non-crossover classes are white bar and eosin, which are written under the symbol $\frac{w \quad B'}{w^e}$. The crossover classes, white and eosin bar, are written to the right under the symbol $\frac{w}{w^e \mid B'}$.

In a second experiment an eosin female was outcrossed to white males.

The regular daughters, white-eosin compounds, were tested by mating to bar males.

TABLE 4

The offspring given by an eosin exceptional female when outcrossed to white males.

No.	Regular offspring		Exceptions		Percent of exceptions
	w-w^e♀	w^e♂	w^e♀	w♂	
98n	56	65	6	7	9.7

TABLE 5

The two kinds of results given by the regular daughters of table 4 when tested by bar males.

No.	Regular offspring			Exceptions		Percent of exceptions
	B′ ♀	w♂	w^e♂	w-w^e♀	B′♂	
104n	60	22	19	3	5	7.3
105n	39	17	15	2	2	5.3
106n	56	24	31	5	3	6.7
110n	70	38	37	2	1	2.
112n	9	9	6	2	—	7.7
Total	234	110	108	14	11	5.2
107n	111	48	68	—	—	—
108n	95	53	53	—	—	—
109n	50	24	23	—	—	—
111n	103	56	53	—	—	—
Total	359	181	197	—	—	—

Of the females tested five produced exceptions, and four were normal (table 5). These nine females bring the total of tested females to twenty, of which eleven must have been XXY and nine XX in constitution.

The third experiment differed from the first only in that the wild type regular daughters were tested by bar males instead of by white bar males.

TABLE 6

The offspring given by an eosin exceptional female when outcrossed to wild males.

No.	Regular offspring		Exceptions		Percent of exceptions
	+♀	w^e♂	w^e♀	+♂	
102n	37	38	2	3	6.2

TABLE 7

The two kinds of results given by the regular daughters of table 6 when tested by bar males.

No.	Regular offspring			Exceptions		Percent of exceptions
	B'♀	w^e♂	+♂	+♀	B'♂	
135n	71	32	44	2	1	2.
136n	59	23	20	—	2	2.
146n	103	39	48	3	1	2.1
Total	233	94	112	5	4	2.
131n	83	45	34	—	—	—
132n	49	22	29	—	—	—
133n	79	52	52	—	—	—
134n	105	44	54	—	—	—
151n	67	53	32	—	—	—
Total	383	216	201	—	—	—

Three daughters proved to be XXY, and five XX females, bringing the totals to fourteen of each kind.

The most extensive experiment of this type consisted of the tests by white bar males of the regular daughters from outcrosses of vermilion exceptional females to eosin males.

TABLE 8

The offspring given by vermilion exceptional females when outcrossed to eosin males.

No.	Regular offspring		Exceptions		Percent of exceptions
	+♀	v♂	v♀	w^e♂	
401	87	95	2	1	1.6
448	53	65	2	1	2.5
463	48	37	2	—	2.3
527	111	95	2	—	1.
528	99	76	1	—	.5
611	136	113	3	2	2.
648	95	95	2	4	3.1
Total	629	576	14	8	1.5

TABLE 9

The two kinds of results given by the regular daughters of table 8 when tested by white bar males

No.	Regular daughters		Regular sons				Exceptions		Percent of exceptions
			w^e / v		w^e v / +				
	w-w^e B′	B′	w^e	v	w^e v	+	+♀	w B′♂	
543	51	57	27	29	10	14	2	2	2.1
544	55	56	46	45	15	13	7	6	5.4
545	67	64	55	47	16	12	5	4	3.3
546	60	59	45	48	14	18	10	10	7.9
547	45	51	34	40	16	14	3	3	2.9
548	46	51	32	39	15	13	6	1	3.4
549	35	61	20	49	22	14	2	3	2.4
552	47	64	30	34	13	12	2	2	2.
553	59	70	38	20	17	20	5	2	3.
554	49	49	37	41	16	14	1	2	1.4
600	36	36	27	24	12	8	3	2	3.4 (w^e♀ 1)
601	66	50	40	49	20	26	4	3	2.7
602	78	72	46	51	25	29	7	—	2.3
603	17	21	15	15	5	4	1	1	2.5
604	87	86	54	52	23	18	11	6	5.
606	77	82	62	53	28	21	2	4	1.8
607	58	78	45	49	17	18	1	1	.8
595	41	29	31	28	18	17	4	5	5.2
596	71	77	49	43	21	23	2	3	1.7
597	63	116	67	62	26	28	6	1	1.9
663	42	60	41	39	18	16	3	5	3.6
679	14	25	22	19	8	14	3	2	4.7
713	68	68	45	51	19	21	3	8	3.8
714	66	56	33	37	15	10	2	3	2.3
Total	1298	1438	741	964	409	397	95	79	3.2
542	67	49	45	34	26	14	—	—	—
550	38	37	41	28	15	14	—	—	—
551	63	59	51	56	20	19	—	—	—
555	66	73	45	47	19	18	—	—	—
556	66	59	35	38	11	10	—	—	—
599	27	26	28	16	12	5	—	—	—
605	82	92	50	69	26	30	—	—	—
598	29	24	15	17	8	8	—	—	—
662	73	56	46	57	17	19	—	—	—
675	77	97	51	38	30	25	—	—	—
677	25	30	23	18	6	7	—	—	—
678	21	22	15	12	4	11	—	—	—
Total	634	624	445	430	194	180	—	—	—

Of the thirty-six females tested in this experiment (table 9), twenty-four gave exceptional and twelve gave only regular offspring. This seemed a somewhat large departure from the expected equality, and for a time I suspected that there might be a real excess of XXY females; but that there is no such inequality of the two types is rendered certain by the experiments which follow. Culture 597 gave a peculiar ratio of 116 bar to 63 white-eosin bar daughters, where equality was expected. The cause of this ratio was not discovered, but the tests of three of the white-eosin bar daughters by cherry males showed that these females were XX (see table 10), and they may therefore be included in the final summary.

In another experiment an eosin vermilion exceptional female was outcrossed to wild males, with the result given in table 11. The regular wild type daughters were then tested by bar males. As shown in table 12, three of the daughters were XXY and two were XX females.

Many of the other experiments that were designed to test special points, have at the same time given information upon the ratio of XXY to XX daughters. In table 13, such data are collected under two headings, cultures giving exceptions and those free from exceptions. There were thirty-four XXY and forty-two XX daughters.

TABLE 10

The offspring given by three regular bar daughters from culture 597 when tested by cherry males.

	Regular daughters				Regular sons				Exceptional sons
	w B′		w / B′		w B′		w / B′		
No.	w-w^c B′	+	w-w^c	B′	wB′	+	w	B′	w^c ♂
693	38	38	25	24	27	32	11	19	—
694	37	36	42	31	34	27	17	21	—
695	42	50	38	43	36	53	28	35	—
Total	117	124	105	98	97	112	56	75	—

TABLE 11

The offspring given by an eosin vermilion exceptional daughter when outcrossed to a wild male.

	Regular offspring		Exceptions		Percent of exceptions
No.	+♀	w^{e}v♂	w^{e}v♀	+♂	
891	34	34	—	—	—

TABLE 12

The two kinds of results given by the regular daughters of table 11 when tested by bar males.

	Regular daughters	Regular sons				Exceptions		Percent of exceptions
		w^e v		w^e / v				
No.	B′	w^{e}v	+	w^e	v	+♀	B′♂	
1056	107	35	31	27	15	1	2	1.4
1058	52	27	17	10	10	—	4	3.3
1059	80	21	24	10	11	12	3	9.3
Total	239	83	72	47	36	13	9	4.4
1057	134	30	26	18	20	—	—	—
1060	89	26	34	17	20	—	—	—
Total	223	56	60	35	40	—	—	—

TABLE 13

The two kinds of results given by the regular daughters from various other experiments when tested by appropriate males.

Giving exceptions (XXY)						No exceptions (XX)				
	Regular offspring		Exceptions			Regular offspring			Exceptions	
No.	♀♀	♂♂	♀♀	♂♂	Percent	No.	♀♀	♂♂	♀♀	♂♂
931	80	112	1	1	1.	730	80	73	—	—
932	77	74	11	13	13.7	777	156	159	—	—
933	113	112	11	8	7.8	818	141	154	—	—
778	144	166	1	1	.6	820	171	193	—	—
819	143	123	1	4	1.8	768	132	141	—	—
815	175	143	4	5	2.8	816	140	168	—	—
817	160	162	1	3	1.2	793	275	280	—	—
770	88	81	—	3	1.7	794	294	285	—	—
839	201	187	1	3	1.	830	141	184	—	—
887	102	92	1	2	1.5	888	105	98	—	—
923	67	65	1	—	.8	889	63	63	—	—
842	151	149	3	9	3.9	890	264	267	—	—
845	115	159	5	6	3.9	892	160	130	—	—
896	177	165	1	—	.3	922	136	141	—	—
897	163	154	2	3	1.6	893	108	111	—	—
912	178	186	4	5	2.4	894	110	123	—	—
915	185	161	—	1	.3	895	178	153	—	—
917	187	184	2	1	.8	911	210	190	—	—
934	69	99	4	1	2.9	913	182	188	—	—
846	117	97	4	1	2.3	914	106	106	—	—
849	129	146	11	12	7.7	916	190	225	—	—
919	191	185	3	6	2.3	847	173	172	—	—
920	82	90	4	—	2.3	848	185	171	—	—
1182	89	76	4	4	4.6	851	144	116	—	—
1205	26	20	3	4	13.2	853	166	152	—	—
1217	116	108	9	5	5.9	898	115	86	—	—
1221	97	79	7	6	6.9	918	67	46	—	—
1206	15	14	1	5	16.6	1203	91	70	—	—
1164	30	19	20	15	41.6	1183	78	76	—	—
1140	154	158	8	7	4.6	1163	108	108	—	—
1148	74	57	4	3	5.1	1185	85	110	—	—
1122	123	92	7	3	4.4	1154	40	49	—	—
1135	113	122	12	5	6.7	1155	190	149	—	—
1138	125	129	12	4	3.9	1198	139	108	—	—
						1212	78	62	—	—
						1141	93	102	—	—
						1147	143	122	—	—
						1123	49	86	—	—
						1133	74	72	—	—
						1134	104	79	—	—
						1139	43	47	—	—
						1233	196	201	—	—

Table 14 gives a few more cultures of the same nature as those given in table 13; but here the males used in testing were such that only among the sons could exceptions be distinguished from the regular offspring. Five females were XXY and six XX.

TABLE 14

The two kinds of results given by regular daughters;—cases where exceptions could be seen only among the sons.

Giving exceptions (XXY)					No exceptions (XX)			
	Regular offspring		Exceptions		Regular offspring			Exceptions
No.	♀	♂	♂	Percent	No.	♀	♂	♂
170n	36	23	1	4.2	171n	32	22	—
173n	112	78	4	4.9	172n	100	79	—
174n	49	57	4	6.1	1257	59	62	—
771	139	127	4	3.1	1255	91	73	—
1256	207	187	9	4.6	1254	83	59	—
					1410	71	77	—

As the summary in table 15 shows, there have been eighty cultures giving exceptions and seventy-nine free from exceptions.

TABLE 15

Summary of the XXY and XX cultures.

Table	XXY	XX
2	5	5
3	1	—
5	5	4
7	3	5
9	24	12
10	—	3
12	3	2
13	34	42
14	5	6
Total	80	79

If the daughters which give exceptions do so because of the presence of a Y chromosome, then it must be concluded from this evidence that the two types XXY and XX are equally frequent (see fig. 6). This means that in reductions of the X-XY type it is a matter of chance whether the extra Y remains in the egg or passes to the polar body, so that XY and X eggs are formed in equal numbers.

THE EQUALITY OF XYY AND XY MALES AMONG THE REGULAR SONS OF XXY FEMALES

In the last section, the daughters produced by the fertilization of X and XY eggs by X sperm were studied, and it was demonstrated that these eggs were equally numerous. A corresponding equality of regular sons of the two types XY (fig. 6 (7)) and XYY (8) must result from the fertilization of these eggs by Y sperm. It is far more difficult to determine this ratio of X to XY eggs by tests of the equality of XY and XYY sons than it is to test this same ratio by means of the XX and XXY daughters. Only enough of the regular sons have been tested to demonstrate the existence of the two types and to show that they are approximately in equal numbers.

SECONDARY NON-DISJUNCTION IN THE MALE

In the spermatogenesis of an XYY male there are two possible methods of synapsis, the XY and the YY types. If the synapses are not preferential but take place according to chance, there should be twice as many XY as YY synapses. At the reduction division the two chromosomes that have synapsed disjoin and go into different cells, while the unsynapsed chromosome goes equally often with each of the other two. Thus after XY synapsis, X and Y disjoin and the free Y goes as often with the Y (X-YY type) as with the X (XY-Y type). In spermatogenesis both cells produced by the reduction division give rise to sperm, so that the X-YY type must produce an equality of XY and Y sperm. As a result of reduction there are four classes of sperm, two small classes, X and YY, from heterosynapsis, and two classes, XY and Y, twice as large and coming from two sources. Obviously there is no chance for the production of exceptions in F_1 through the fertilization of the normal X eggs of an XX female by any of the four kinds of sperm of the XYY male. For example, as figure 8 shows, only the expected wild type daughters and sable sons result from the fertilization of an ordinary sable female by a vermilion XYY male.

The wild type daughters of an XYY male are expected to be of two kinds, XX daughters (figure 8, 1) from the X sperm, and XXY daughters (3) from the XY sperm. It has been shown that females having the constitution XXY produce secondary exceptions, both when they are matroclinous exceptions and when they are regular daughters. Of still another origin are these XXY daughters of an XYY male, but these also should produce secondary exceptions if the presence of the extra Y is the cause of such exceptions.

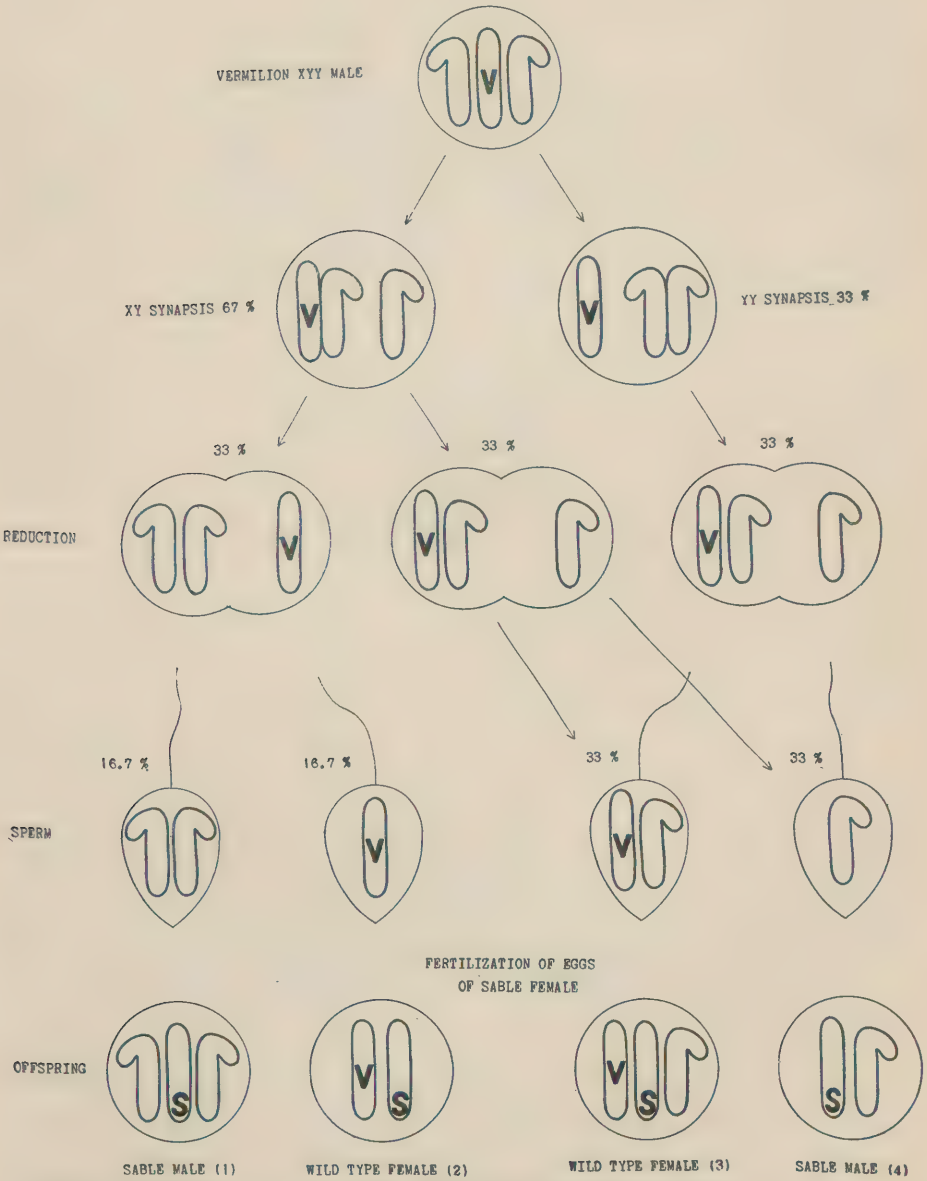


FIGURE 8. Diagram of secondary non-disjunction in the male. Four kinds of sperm are produced, but none of these lead to the production of exceptions in F_1.

If synapsis is according to chance, twice as many daughters of an XYY male should produce exceptions as do not. From the actual percentage of XX daughters a calculation of the amount of XY synapsis can be made.

In the first set of experiments to test the points just indicated, three eosin regular sons (from outcrosses of eosin exceptional females by white males) were outcrossed to white females. There were no exceptions in F_1, as is shown in table 16. Some of the white-eosin regular daughters from each culture were tested by white bar males. As table 17 shows, two of the three sets (*A* and *B*) gave exceptions, while the other set (*C*) gave no exceptions.

TABLE 16

The results given when three eosin regular sons were outcrossed to white females.

No.	w-w^e♀	w^e♂
44n	77	93
100n	157	122
101n	95	91
Total	329	306

TABLE 17

A. The two kinds of results given by the wild type daughters from culture 44n when tested by white bar males.

No.	Regular offspring				Exceptions		Percent
	wB′♀	w-w^{e}B′♀	w♂	w^e♂	w-w^e♀	wB′♂	
46n	54	50	54	52	6	1	3.2
48n	54	48	57	54	5	3	3.6
49n	56	54	51	60	1	4	2.2
Total	164	152	162	166	12	8	—
45n	59	59	61	62	—	—	—
47n	68	72	58	55	—	—	—
Total	127	131	119	117	—	—	—

B. Daughters from culture 100n.

115n	44	32	36	33	9	4	8.2
116n	25	27	21	28	12	5	15.3
117n	52	55	66	51	7	16	9.4
118n	31	37	30	37	10	5	10.
125n	27	34	27	23	6	5	9.
126n	9	8	14	13	6	2	15.3
129n	39	35	45	26	9	3	7.6
Total	227	228	239	211	59	40	—
113n	36	53	51	57	—	—	—
114n	36	57	50	50	—	—	—
127n	40	43	45	38	—	—	—
130n	27	31	22	30	—	—	—
Total	139	184	168	175	—	—	—

C. Daughters from culture 101n

137n	43	40	39	42	—	—	—
138n	38	30	39	25	—	—	—
143n	37	31	30	30	—	—	—
144n	20	18	24	24	—	—	—
147n	43	38	24	43	—	—	—
148n	26	20	30	31	—	—	—
149n	37	43	22	30	—	—	—
150n	38	34	33	39	—	—	—
Total	282	254	241	264	—	—	—

In another experiment a single eosin regular son was outcrossed to bar females (table 18). Of the seven regular daughters tested by vermilion sable males, none gave exceptions (table 19).

TABLE 18

The offspring given by an eosin regular son when outcrossed to bar females.

No.	B′♀	B′♂
175n	67	75

TABLE 19

The results given by the wild type daughters from culture 175n when tested by vermilion sable males.

No.	Regular offspring ♀♀	Regular offspring ♂♂	Exceptions v s ♂
190n	21	21	—
191n	56	50	—
192n	40	48	—
193n	67	66	—
194n	56	57	—
195n	59	48	—
196n	50	48	—
Total	349	338	—

In the next experiment four eosin regular sons were outcrossed to wild females (table 20).

Some of the wild type regular daughters from each of these cultures were tested by vermilion miniature males. As table 21 shows, one of the four sets gave exceptions, while the other three sets gave no exceptions.

TABLE 20

The offspring given by four eosin regular sons when outcrossed to wild females.

No.	+♀	+♂
8	94	95
5	74	64
6	70	69
7	76	68
Total	314	296

TABLE 21

A. The results given by wild type daughters from culture 8 when tested by vermilion miniature males.

No.	Regular offspring ♀♀	Regular offspring ♂♂	Exceptions v m ♂
52	17	19	2
53	121	103	9
57	125	103	7
58	144	133	1
Total	407	359	19
54	126	109	—
55	60	44	—
56	90	86	—
Total	276	239	—

B. Daughters from culture 5.

35	51	44	—
36	43	47	—
37	45	36	—
38	125	117	—
39	74	64	—
	338	308	—

C. Daughters from culture 6.

41	44	52	—
42	23	28	—
44	57	49	—
45	46	43	—
45.1	73	75	—
Total	243	247	—

D. Daughters from culture 7.

46	92	97	—
47	85	81	—
48	49	42	—
49	67	51	—
50	61	52	—
51	34	43	—
Total	388	366	—

In another experiment vermilion regular sons were outcrossed to eosin females (table 22), and the daughters were tested by bar males. All of the sets gave exceptions (table 23) showing that all five regular sons had been XYY.

TABLE 22

The results given by five vermilion regular sons when outcrossed to eosin females.

No.	+♀	w^e♂
733	45	41
724	68	70
723	76	87
726	63	56
734	61	73
Total	313	327

TABLE 23

A. The results given by the regular daughters from culture 733 when tested by bar males.

No.	Regular daughters	Regular sons				Exceptions		Percent of exceptions
		w^e — v		w^e | v				
	B′	w^ev	+	w^e	v	+♀	B′♂	
803	17	3	2	3	2	1	—	3.6
805	171	57	53	39	26	4	2	1.7
806	150	41	44	20	26	1	4	1.7
807	44	11	13	9	12	1	1	2.2
808	132	43	53	20	22	1	4	1.8
809	54	23	16	9	7	1	1	1.8
Total	568	178	181	100	95	9	12	

B. Daughters from culture 724 tested by white bar males.

779	77	66	36	48	24	27	4	6	3.5
781	13	21	6	10	4	4	2	2	6.5
782	65	57	41	28	17	27	—	3	1.3
Total	155	144	83	86	45	58	6	11	—
780	59	60	27	27	14	13	—	—	—
814	37	46	28	27	21	35	—	—	—
Total	96	106	55	54	35	48	—	—	—

C. Daughters from culture 723 tested by white bar males.

825	66	38	33	29	14	17	4 —	2.
826	46	35	24	26	13	15	3 —	1.9
Total	112	73	57	55	27	32	7 —	

D. Daughters from culture 726 tested by white bar males.

784	65	67	37	40	18	18	3 3	2.4
785	97	84	69	77	32	36	6 7	3.2 (w^e♀1)
786	110	113	68	61	40	34	4 4	1.8
827	72	92	55	56	29	25	4 4	2.4
Total	344	356	229	234	119	113	17 18	—
783	44	52	33	51	17	16	— —	—
828	113	113	78	69	34	30	— —	—
Total	157	165	111	120	51	46	— —	

E. Daughters from culture 734 tested by white bar males.

831	36	34	17	27	17	11	— 1	.7
832	60	51	46	36	14	15	1 1	.9
834	11	8	9	6	5	4	1 —	2.3 (w^e♀1)
Total	107	93	72	69	36	30	2 2	
833	13	20	11	10	4	3	— —	—

Cultures 785 and 834 each produced an eosin female. These are examples of equational non-disjunction, and will be very fully discussed later.

In the final experiment, a yellow eosin vermilion regular son was outcrossed to wild females (table 24). The daughters were tested by bar males (table 25).

TABLE 24

The offspring given by a yellow eosin vermilion regular son when outcrossed to wild females.

No.	+♀	+♂
1461	69	73

TABLE 25

The offspring given by the wild type daughters from culture 1461 when tested by bar males

No.	Regular daughters	y w^e v		y / w^e v		y w^e / v		y / w^e v		Exceptions		Percent of exceptions
	B′	y w^ev	+	y	w^ev	y w^e	v	yv	w^e	+♀	B′♂	
1634	55	21	36	—	—	6	17	—	—	3	6	6.2
1635	124	34	32	2	2	15	14	1	—	12	12	9.7
1637	135	29	46	—	1	12	22	—	1	13	14	9.9
1638	81	26	31	—	—	9	6	—	—	16	16	17.3
1657	161	38	48	1	1	21	13	—	—	12	15	9.0 (yw^e♀1)
1658	99	41	43	—	—	11	13	—	—	17	23	16.2
1659	63	31	35	—	—	8	5	—	—	10	11	12.9
Total	718	220	271	3	4	82	90	1	1	83	97	
1656	36	14	16	—	—	4	4	—	—	—	—	—

All except one of the eight daughters tested gave exceptions. The percentages of exceptions given by the cultures of table 25 were unusually high.

TABLE 26

A summary of the tests of the regular sons classified as XYY if their daughters gave exceptions, and as XY if they gave none.

From XYY male			From XY male		
Origin	XXY daughters	XX daughters	Origin	XXY daughters	XX daughters
44n	3	2	101n	—	8
100n	7	4	175n	—	7
8	4	3	5	—	5
733	6	—	6	—	5
724	3	2	7	—	6
723	2	—			
726	4	2			
734	3	1			
1461	7	1			
9XYY♂♂	39	15	5XY♂♂	—	31

As shown in the summary of table 26, fourteen regular sons have been outcrossed and tested through tests of their daughters. Five of these sons must have been ordinary XY males, since none of their daughters gave exceptions. Nine sons must have been XYY in composition, since some of the daughters from each gave exceptions. This ratio of 9:5 must be considered as only a chance deviation from equality since these two classes of sons were produced by the same process which has been shown to produce two classes of daughters in equal numbers.

The results given by the daughters of the nine XYY males show that many more of these daughters must have been XXY than were XX. Out of a total of fifty-four such daughters tested, only fifteen, or twenty-eight percent gave no exceptions.

If the synapses in an XYY male take place according to chance, there should be 67 percent of XY synapsis (heterosynapsis) and 33 percent of YY synapsis (homosynapsis). Since in this section we have been testing only the daughters of XYY males, the calculation can be narrowed to the ratio of X to XY sperm which should follow various percents of XY synapsis. The X-bearing sperm from the cases of XY synapsis should be half XY and half X, while from homosynapsis all should be XY, that is, 33 percent of the X-bearing sperm should produce XX daughters and 67 percent XXY daughters. If all synapses are XY then 50 percent of the "female-producing" sperm are X. Among the female-producing sperm the percent of X sperm (y) which follow various percentages of heterosynapsis (x) can be found by the simple formula $y = \frac{x}{2}$. The realized value of 28 percent of X sperm suggests that the synapses are according to chance, which would give 33 percent of X sperm. In an XYY male the synapsis coefficient of X (c) in terms of Y (100) is expressed by the formula $c = \frac{50\,y}{50 - y}$.

THE CONSTITUTION OF THE PATROCLINOUS SONS OF XXY FEMALES

The usual method by which males are produced is by the fertilization of X eggs by Y sperm; but if our analysis of secondary non-disjunction is correct the patroclinous sons are produced by a method the exact reverse of this—*by the fertilization of Y eggs by X sperm* (see figure 6). Such males are XY in composition and should therefore behave in heredity exactly like ordinary males. They should be able neither to produce exceptions nor to transmit the power of producing exceptions.

In order to test this conclusion, three eosin exceptional sons (from

outcrosses of vermilion exceptional females to eosin males) were outcrossed to vermilion females. The offspring consisted of the expected wild type daughters and vermilion sons, as shown in table 27. Some of the wild type daughters from each male were tested by bar males, with the results shown in table 28.

TABLE 27

The offspring given by three eosin exceptional sons when outcrossed to vermilion females.

No.	+♀	v♂
698	116	94
666	96	91
729	105	82
Total	307	267

TABLE 28

A. The offspring given by wild type daughters from culture 698 when tested by white bar males.

	Regular daughters		Regular sons				Exceptions	
			w^e / v		w^e / +	v		
No.	w-w^eB′	B′	w^e	v	w^ev	+	+♀	wB′♂
759	76	107	52	58	32	32	—	—
760	83	71	60	64	28	25	—	—
761	77	74	56	53	19	30	1	—
762	89	71	44	50	21	34	—	—
763	73	70	46	43	18	27	—	—
764	61	61	37	36	16	19	—	1 (Sterile)
765	81	75	61	67	36	18	—	1 (Sterile)
Total	540	519	356	371	170	185	1	2
B. Daughters from culture 666.								
738	89	87	66	59	17	28	—	—
739	86	78	63	60	19	25	—	—
740	44	49	25	31	21	14	—	—
741	91	107	61	57	25	27	—	—
742	83	81	36	63	23	22	—	—
743	92	87	80	81	14	29	—	2
744	43	45	26	27	9	11	—	—
745	85	99	73	70	20	27	—	—
Total	613	633	430	448	148	183	—	2

C. Daughters from culture 729.

787	139	140	95	78	50	38	1	—	
788	124	114	83	73	42	30	1	—	
789	140	140	87	82	37	56	—	—	
790	121	133	98	74	51	27	—	—	
791	111	101	61	73	28	28	—	—	
792	113	108	87	80	40	45	—	—	
829	118	123	90	73	34	32	—	—	(w^e ♀ 1)
Total	866	859	601	532	282	256	2	—	(w^e ♀ 1)

Of the twenty-two daughters tested, fifteen produced no exceptions. In culture 743 there were two white bar males present on the first day of hatching; but unfortunately there is some doubt as to whether these males were parents which had escaped being thrown out, or were exceptional sons; the probability is that they were exceptions. There is no doubt that in six other cultures genuine exceptions occurred. The analysis had led to the inference that an exceptional son can not transmit to his daughters the power of producing exceptions. What then is the explanation of these real exceptions?

It seemed most probable that these exceptions were all primary, and not due to the presence of an extra Y in the females tested. It is very striking that in spite of the unusually large output of the cultures of table 28 only one (and this the somewhat doubtful one), produced more than a single exception. As already shown by the tables in which secondary non-disjunction occurs, such a very low production of exceptions would be most unusual for a like number of XXY females. In this respect these tables are in marked contrast to those in the last section.

The exception in culture 829 was an eosin daughter and is another example of the rather rare equational non-disjunction to be discussed later. In the case of culture 829 there is direct evidence showing that the mother did not have a Y chromosome and that the exception is primary. We have seen that half the daughters of an XXY female are themselves XXY and in turn produce exceptions. As shown in Table 29 the daughters from culture 829 did not fulfill this condition, and therefore the mother of culture 829 was not XXY.

Seven of the eight daughters of 829 gave no exceptions at all and must therefore have been simply XX in composition; the remaining daughter gave a single patroclinous son. This son proved to be absolutely sterile, from which test we may conclude that he was a primary exception from an XX mother; for, as will be shown later, primary

TABLE 29

The offspring given by the white-eosin bar regular daughters from culture 829 when tested by miniature males.

No.	Regular daughters	Regular sons: w/w^e B′ wB′	Regular sons: w/w^e B′ w^e	Regular sons: w w^e/B′ w	Regular sons: w w^e/B′ w^eB'	Exceptions: w-w^eB′♀	Exceptions: m♂
980	74	25	16	16	10	—	—
981	77	17	22	26	17	—	—
982	73	19	18	13	12	—	—
983	119	31	26	20	30	—	—
984	58	16	19	15	12	—	1 (Sterile)
Total	401	108	101	90	81	—	1
		All regular sons.					
985	156	156				—	—
986	119	115				—	—
987	113	102				—	—
Total	388	373				—	—

male exceptions with the formula XO are totally sterile. If this single exception was primary, then none of the eight daughters from culture 829 was an XXY female, and this result shows that the mother of 829 was simply XX; the chances are 255 to 1 that one of the eight daughters would have been XXY if the mother were XXY.

The same test that was used in the case of culture 829 was applied to culture 788, another of the seven cultures of table 28 which gave exceptions.

TABLE 30

The offspring given by the white-eosin bar regular daughters from culture 788 when tested by miniature males.

No.	Regular daughters	Regular sons: w/w^e B′ wB′	Regular sons: w/w^e B′ w^e	Regular sons: w w^e/B′ w	Regular sons: w w^e/B′ w^eB'	Exceptions: w-w^eB′♀	Exceptions: m♂
1012	151	35	27	35	27	—	—

All regular sons.

1013	26	28	—	—
1014	130	128	—	1 (Sterile)
Total	156	156	—	1

One of three daughters from culture 788 gave a single patroclinous son which was sterile and presumably therefore a primary exception (table 30). None of the three daughters were XXY and this suggests (chances 7 to 1) that their mother was not XXY.

The exceptional males of cultures 764 and 765, table 28, were both sterile and agree therefore with the expectation for primary exceptions.

These tests have shown that four out of the six undoubted exceptions were primary and lead to the belief that the other exceptions were also primary.

In a second experiment the exceptional son tested was a yellow male from an outcross of an eosin exceptional female to a yellow male. This son was outcrossed to a white female (table 31) and his wild type daughters were tested by bar males (table 32).

TABLE 31

The offspring given by an exceptional yellow son when outcrossed to white females.

No.	+♀	w♂
928	113	106

TABLE 32

The offspring given by the wild type daughters from culture 928 when tested by bar males.

	Regular offspring	Exceptions	
No.	♀♀ and ♂♂	+♀	B′♂
1049	20	—	—
1050	129	—	—
1051	237	—	—
1052	131	—	—
1053	39	—	—
1054	106	—	—
1055	58	—	—
Total	720	—	—

As shown by table 32 none of the seven daughters gave any exceptions.

In the final experiment, six sable forked exceptional sons were outcrossed to eosin vermilion females (table 33), and the daughters were tested by bar males. As shown by table 34, there is here no question of secondary non-disjunction. Only two cultures from a total of forty-six gave exceptions, and these were primary, as the results in the sister cultures prove.

TABLE 33

The offspring given by six sable forked exceptional sons when outcrossed to eosin vermilion females.

No.	+♀	w^e v♂
1213	61	43
1214	89	82
1225	63	46
1226	147	153
1232	97	80
Total	465	411

TABLE 34

A. The offspring given by the wild type daughters from culture 1213 when tested by bar males.

No.	Regular daughters	Regular sons																		Exceptions	
		w^e v	sf	w^e sf v		w^e v sf +		w^ev f s		w^e v sf		w^e s v f		w^ev s f		w^e v s f		+♀	B′
	B′	w^ev	sf	w^esf	v	w^evsf	+	w^evf	s	w^e	vsf	w^es	vf	w^evs	f	w^ef	vs		
1320	100	21	27	12	14	4	6	–	–	1	3	–	–	–	–	-	-	-	-
1321	97	14	29	7	13	4	5	2	6	–	–	–	2	–	–	-	-	-	-
1322	44	14	9	3	6	1	2	6	3	–	1	–	–	–	–	-	-	-	-
1323	54	8	13	4	7	2	4	4	2	–	–	–	–	–	–	-	-	-	-
1324	116	27	27	2	–	3	3	7	5	1	–	2	–	–	1	-	-	-	-
1337	94	22	13	4	15	1	5	1	2	–	–	1	1	1	–	-	-	-	-
1338	34	1	14	1	5	–	–	–	3	–	–	–	1	–	–	-	-	-	-
1339	67	16	16	8	3	1	2	6	3	1	–	–	2	1	–	-	-	-	-
1340	104	18	26	9	16	3	6	5	–	–	2	–	–	–	–	-	-	-	-
Total	710	141	174	50	79	19	33	35	31	3	6	3	6	2	1	-	-	-	-

B. Daughters from culture 1214.

1325	113	38	20	–	3	3	4	4	7	1	–	–	3	–	–	-	-	1	-	
1326	119	28	23	19	19	2	7	9	2	–	3	2	–	–	–	-	-	-	-	
1327	161	50	51	14	22	3	8	9	6	–	1	3	2	–	–	-	-	-	-	
1328	159	24	39	21	18	5	5	12	10	1	1	–	2	–	–	-	-	-	-	
1342	93	24	21	6	7	2	3	5	5	–	–	–	–	–	–	-	-	-	-	
1343	73	12	16	7	4	2	5	–	4	–	–	–	–	–	–	-	-	-	-	
1344	51	16	10	8	8	–	3	3	2	–	1	2	–	–	–	-	-	-	-	
1345	56	19	12	5	9	3	1	3	5	–	–	1	1	–	–	-	-	-	-	
1346	171	42	33	10	22	8	5	9	4	2	1	2	2	–	–	-	-	-	-	
Total	996	253	225	90	112	28	41	54	45	4	7	10	10	–	–	-	-	1	-	

C. Daughters from culture 1225.

1335	72	37	24	6	15	4	3	5	3	–	-	–	1	–	–	-	-	-	-	
1347	131	32	20	15	23	2	8	5	3	–	–	1	2	–	1	-	-	-	-	
1348	184	34	49	23	20	4	7	8	2	2	1	1	1	–	–	-	-	-	-	
1349	172	39	30	13	20	10	7	3	7	–	–	2	–	–	–	-	-	-	-	
1350	228	46	49	19	27	2	9	12	7	1	2	–	1	–	1	-	-	-	-	
1372	194	43	31	9	19	2	12	10	9	1	–	1	–	–	1	-	-	-	-	
Total	981	231	193	85	124	24	46	43	31	4	3	5	5	–	3	-	-	-	-	

D. Daughters from culture 1226.

1351	183	37	48	16	19	8	12	10	4	1	2	2	2	–	–	-	-	-	-	
1373	117	29	15	6	6	–	4	3	4	–	1	–	–	–	–	-	-	-	-	
1374	103	24	20	6	10	–	5	8	3	–	1	–	1	–	–	-	-	-	-	
1375	89	19	12	2	12	1	6	4	2	–	–	–	1	–	–	-	-	-	-	
1376	110	37	17	3	18	2	3	3	7	1	–	1	–	–	–	-	-	-	-	
1377	123	33	26	15	24	5	7	5	7	2	2	3	4	1	-	-	-	-	-	
1378	71	14	5	6	6	3	6	5	–	–	–	2	1	-	-	-	-	-	-	
1379	101	35	17	14	17	8	6	9	6	–	1	1	–	-	-	-	-	-	-	
1380	178	44	46	25	27	6	6	13	12	5	–	1	5	-	-	-	-	-	-	
1424	59	17	23	2	7	2	4	4	4	–	–	2	1	-	-	-	-	1	-	(w^{e}v♀1)
1425	40	55	6	3	2	–	1	3	1	–	–	–	–	-	-	-	-	-	-	
1426	157	56	49	28	17	9	7	7	11	1	1	3	2	1	-	-	-	-	-	
1427	42	13	17	6	5	3	–	1	2	1	–	1	–	-	-	-	-	-	-	
1428	73	12	13	8	11	–	3	1	4	–	–	1	1	-	-	-	-	-	-	
1430	24	4	4	3	4	1	–	–	1	–	–	1	–	-	-	-	-	-	-	
Total	1470	379	319	143	185	48	70	76	68	11	8	18	18	2	-	-	-	1	-	(w^{e}v♀1)

E. Daughters from culture 1232.

1381	75	12	14	5	9	2	3	3	2	1	–	1	1	-	1	-	-	-	-	
1382	110	22	30	16	23	2	3	6	12	–	–	–	2	-	-	-	-	-	-	
1397	190	44	45	28	14	4	3	9	11	1	–	2	3	-	-	-	-	-	-	
1398	147	34	40	9	8	3	3	3	10	1	–	1	1	-	-	-	-	-	-	
1399	198	65	53	37	26	6	8	13	10	11	–	4	2	-	-	-	-	-	-	
Total	720	177	182	95	80	17	20	34	45	4	–	8	9	-	1	-	-	-	-	

F. Daughters from culture 1268.

1401	114	22	22	12	17	5	10	6	3	1	1	4	3	-	1	-	-	-	-	
1402	142	39	32	10	11	3	6	4	4	3	–	–	1	1	-	-	-	-	-	
Total	256	61	54	22	28	8	16	10	7	4	1	4	4	1	1	-	-	-	-	

TABLE 35

Summary of the results given by the daughters of exceptional sons.

Parentage	Exceptions absent	Primary exceptions
698	4	3
666	7	1
729	4	3
728	7	—
1213	9	—
1214	8	1
1225	6	—
1226	14	1
1232	5	—
1268	2	—
Ten tested	66	9

As the summary of table 35 shows, no exceptions at all appeared in sixty-six of the seventy-five cultures from daughters of exceptional sons. The exceptions which appeared in the other nine cultures may in one case be due to error (though this is not probable), and in the case of six others tests have been made which show the exceptions to have been primary. If all these exceptions were primary, as there seems no reason to doubt, then we may conclude that the exceptional sons do not transmit the power of producing secondary exceptions, and that their composition is simply XY.

XO MALES AND PRIMARY NON-DISJUNCTION

It is evident from the results of the previous section that primary non-disjunction occurring in the female is not extremely rare. There were twelve primary exceptions among the 20,484 flies which were descended from patroclinous sons. This is one in 1700. The actual number of occurrences of primary non-disjunction must have been twice as frequent since half the non-disjunctional eggs are lost as XXX and YY zygotes.

All exceptional daughters produced by primary non-disjunction should receive XX from the mother and Y from the father and should therefore produce secondary exceptions. The primary matroclinous daughter in culture 761, table 28, was tested upon this point by outcrossing to white bar males. The offspring showed that she was XXY as expected.

TABLE 35A

The offspring given by a primary matroclinous wild type daughter from culture 761 when tested by white bar males.

	Regular daughters		Regular sons				Exceptions		Percent of exceptions
			$\frac{w^e}{v}$		$\frac{w^e}{+}$	$\frac{v}{+}$			
No.	w-w^eB′	B′	w^e	v	w^ev	+	+♀	wB′♂	
886	88	79	83	47	29	38	5	7	3.2

The fact that XO males are totally sterile is of unusual interest since it is the first indication that the Y chromosome is something more than a gear wheel in the mechanism of synapsis and reduction. The evidence of this paper proves that the Y has no effect upon the sex or the sex-linked characters of either the male or female, but that the Y does play some positive rôle is proved by the fact that XY males are fertile and XO males are sterile.

THE INDEPENDENCE OF NON-DISJUNCTION

So far, the evidence has been treated upon the basis that secondary non-disjunction is caused by the presence of an extra Y chromosome, but practically all of the data given thus far might equally well be explained by the assumption of a *dominant* sex-linked gene. This hypothesis could be easily tested by finding the linkage relations of such a gene with other sex-linked genes. The amounts of crossing over between non-disjunction and each other gene should be consistent with its occupying a definite position in the X chromosome. The actual experiment showed that non-disjunction is independent of all the known sex-linked genes and can not therefore be due to a gene carried by the X chromosome.

On this view, a vermilion exceptional female must be supposed to have the gene for non-disjunction in at least one of her two X chromosomes. If such a female is mated to an ordinary eosin male, all the regular daughters should be heterozygous for eosin and vermilion and half should be heterozygous for non-disjunction also. The daughters carrying non-disjunction can be picked out because they give exceptions. Table 9 already given on page 23 gives the tests of many such females.

Any exceptional daughter given by such a culture should be an exact duplicate of her mother, that is, she should be heterozygous for eosin, vermilion, and non-disjunction. The offspring of such a female will

show by the proportions of the various classes the amount of crossing over between non-disjunction and eosin and between non-disjunction and vermilion. We can easily enough classify the offspring with respect to the eye-colors eosin and vermilion, but to determine whether any particular fly carries non-disjunction it is necessary to test for exceptions.

The first step of the experiment to test the linkage of non-disjunction was to cross an exceptional female from table 9 by an eosin tan vermilion male.

TABLE 36

The offspring given by four wild type exceptional daughters heterozygous for eosin, vermilion, and non-disjunction when crossed to eosin tan vermilion males.

	Daughters				Regular sons				Exceptional sons	
	$\frac{w^e}{v}$		$\frac{w^e}{v}$ | v		$\frac{w^e}{v}$		$\frac{w^e}{v}$ | v			
No.	w^e	v	w^ev	+	w^e	v	w^ev	+	w^e t v	Percent
630	29	29	19	20	21	19	8	6	11	16.9
718	27	25	19	20	13	18	7	9	1	2.1
757	65	59	29	45	76	68	23	29	8	3.9
758	61	64	37	35	53	62	34	37	7	3.6
	182	177	93	111	163	167	72	81	27	5.3

The offspring of four such matings are given in table 36. The wild type daughters in this table are of two kinds, namely, exceptional daughters which like the mother are heterozygous for eosin and vermilion, but which do not carry tan (since they received no X from the father), and regular daughters which do carry tan. This last class results from crossing over between eosin and vermilion and each fly must be tested to see whether it carries non-disjunction or not. Table 37 gives the results of the tests of thirty-five of the wild type daughters from table 36.

TABLE 37

The three kinds of results given by the wild type daughters from table 36 when tested by white bar males.

(A) Daughters giving exceptions.

No.	Regular daughters		Regular sons								Exceptions		Percent
			w^e t v		w^e | t v		w^e t | v		w^e | t | v			
	w-w^eB′	B′	w^etv	+	w^e	tv	w^et	v	w^ev	t	+♀	B′♂	
770	39	49	23	26	15	10	2	4	1	—	—	3	1.7
839	111	91	52	57	30	42	2	4	—	—	1	3	1.
842	80	71	54	56	12	15	9	2	1	—	3	9	3.9
845	57	58	48	61	24	16	2	8	—	—	5	6	3.9
846	57	60	38	41	8	6	3	1	—	—	4	1	2.3
849	69	60	52	54	20	12	1	6	1	—	11	12	7.7
896	89	88	67	50	17	19	11	1	—	—	1	—	.3
897	85	78	54	56	13	21	6	4	—	—	2	3	1.6
912	85	93	68	68	27	19	4	—	—	—	4	5	2.4
915	100	85	62	57	17	15	5	5	—	—	—	1	.3
917	97	90	60	76	23	19	5	1	—	—	2	1	.8
919	106	85	59	67	20	26	5	8	—	—	3	6	2.3
920	48	34	31	28	9	15	3	3	—	1	4	—	3.4
934	32	37	24	47	9	12	3	4	—	—	4	1	2.9
Total	1055	978	692	744	244	247	61	51	3	1	44	51	2.3

(B) Daughters giving no exceptions.

730	40	40	25	37	—	5	5	1	—	—	—	—	—
793	129	146	99	94	29	34	16	7	—	1	—	—	—
794	147	147	90	83	49	46	10	6	—	1	—	—	—
830	73	68	57	57	32	33	3	2	—	—	—	—	—
847	93	80	64	63	19	21	—	5	—	—	—	—	—
848	100	85	63	59	22	15	6	5	1	—	—	—	—
851	64	80	51	37	19	7	1	1	—	—	—	—	—
853	87	79	53	55	18	12	7	6	1	—	—	—	—
893	60	48	42	35	8	12	6	6	1	—	—	—	—
894	58	52	53	39	13	14	1	2	1	—	—	—	—
895	86	92	66	50	18	14	4	7	—	—	—	—	—
898	57	58	37	28	11	9	1	—	—	—	—	—	—
911	116	94	59	79	20	23	5	4	—	—	—	—	—
913	85	97	66	72	18	18	8	6	—	—	—	—	—
914	45	61	39	50	4	7	3	3	—	—	—	—	—
916	91	99	77	77	24	39	4	4	—	—	—	—	—
918	39	28	20	10	11	4	—	—	1	—	—	—	—
	1370	1354	962	925	315	312	80	59	5	2	—	—	—

(C) Wild type daughters which were exceptions.

No.	Regular daughters		Regular sons				Exceptions		
			$\frac{w^e}{v}$		$\frac{w^e \quad v}{+}$				
	w-w^{e}B′	B′	w^e	v	w^{e}v	+	+♀	wB′♂	Percent
843	98	83	61	71	23	12	9	8	4.7
844	62	75	50	48	16	21	9	12	7.2
850	64	60	43	40	13	24	3	6	3.6
852	29	31	17	33	6	6	2	6	6.2
Total	253	249	171	192	58	63	23	32	5.3

Of the thirty-five daughters whose tests appear in table 37, four (37 *C*) were matroclinous exceptions and useless for our present purpose. Of the thirty-one females which were crossovers between eosin and vermilion, fourteen, that is, about half, gave exceptions (37 *A*). Non-disjunction entered this experiment in company with vermilion, so that in the production of each of these fourteen females, which did not have vermilion (i.e., were wild type), but which did not produce exceptions there must have been a crossover between vermilion and non-disjunction. There are three general regions in which the gene for non-disjunction might be assumed to be located, namely, to the left of eosin, between eosin and vermilion, and to the right of vermilion. If we assume that non-disjunction is to the right of vermilion then the genes entered the cross in the following way $\frac{w^e}{v \quad N'}$ and a wild type female which produced exceptions must be a double crossover ($\frac{w^e + v +}{N'}$, the egg represented by the lower symbol). A glance at any of the tables, for example tables 45A and 45D, in which double crossing over is recorded will demonstrate how rare an occurrence double crossing over is. But in this experiment we should have to conclude that the double crossovers (14) are practically as numerous as the single crossovers between eosin and vermilion (17), a result that is impossible on the assumption that non-disjunction is due to a gene whose inheritance is similar to the inheritance of other sex-linked genes. We must therefore conclude that a gene for non-disjunction does not lie in the portion of X to the right of vermilion. Likewise if non-disjunction lies to the left of eosin the seventeen wild type females which did not give exceptions must be double crossovers, a frequency of double crossing

over so great as to preclude the possibility of non-disjunction lying to the left of eosin. But if non-disjunction lies about midway between eosin and vermilion then neither of the two kinds of wild type females should be a double crossover. The fourteen normal females should represent single crossing over between eosin and non-disjunction ($\underline{w^e}$ | $\underline{N'}$ $\underline{v}$) and the seventeen non-disjunctional females should represent single crossing over between non-disjunction and vermilion ($\underline{w^e}$ $\underline{N'}$ | $\underline{v}$). This evidence, then, does not exclude the assumption that a gene for non-disjunction lies about midway between eosin and vermilion, though it does exclude the possibility of such a gene lying in any other position in the X. The evidence in the next section will show that non-disjunction can not lie even in this position midway between eosin and vermilion.

On the other hand the evidence in this section is entirely consistent with the assumption that the cause of the secondary exceptions is the presence of the Y chromosome in an XXY female. Exactly this realized result is expected if non-disjunction is independent of all sex-linked genes. The equality of wild type daughters carrying non-disjunction and free from non-disjunction is due to the free assortment of the Y from that X with which it entered the XXY zygote, and proves the important point that the Y synapses with and assorts from the two X chromosomes (X and X′) according to chance.

ATTEMPTS TO OBTAIN PURE STOCK OF NON-DISJUNCTION

The history of the various attempts to obtain a stock where every female should give exceptions when outcrossed, furnishes a new line of evidence to prove that a sex-linked gene cannot be the cause of secondary non-disjunction.

The first view that had presented itself was that non-disjunction was due to a recessive gene carried by the X chromosome. Since both the X chromosomes of a non-disjunctional female are transmitted intact to her exceptional daughters, every exceptional daughter would remain homozygous for such a gene. Likewise all the regular sons of such females should receive the gene. If this were true, mating an eosin exceptional female to her eosin regular brothers would give the required stock. However, tests of females of a stock obtained in this way showed that only about three quarters of them produced exceptions.

A possible explanation of this failure to obtain pure stock came with the discovery that half of the regular daughters of an exceptional female produce exceptions. The cause of the phenomenon was then thought to be a dominant rather than a recessive gene.

In attempting to secure a pure stock, a general method was used which enables one to follow a given chromosome through some generations with the certainty that it will emerge intact—that whatever genes were in it originally will still be in it, and that no others will have been switched in by crossing over.

The whereabouts in the X chromosome of the gene for non-disjunction was assumed to be unknown, so that the method was devised to guard the whole length of the X chromosome against escape of the gene while the stock was being made. The first step was to mate an eosin exceptional female, by hypothesis heterozygous for non-disjunction, to a yellow vermilion bar male:

TABLE 38

The results given by two eosin exceptional daughters outcrossed to yellow vermilion bar males.

No.	Regular offspring		Exceptions		Percent of exceptions
	B'♀	w^e♂	w^e♀	yvB'♂	
165n	68	75	7	4	7.1
166n	66	56	11	11	15.3
Total	134	131	18	15	

Half the regular bar daughters of this cross have a maternal chromosome bearing eosin and non-disjunction and can be picked out because they give exceptions. In table 39 are the results given by five

TABLE 39

The two kinds of results given by five bar regular daughters from table 38 when tested by yellow vermilion forked males.

No.	Daughters	Regular sons	Exceptional sons	
			yvp♂	Percent
170n	36	23	1	4.2
173n	112	78	4	4.9
174n	49	57	4	6.6
Total	197	158	9	—
171n	32	22	—	—
172n	100	79	—	—
	132	101	—	—

daughters when tested by yellow vermilion *forked* males (forked is only half a unit from bar). Eosin sons which have retained non-disjunction can be selected from the cultures which gave exceptions by the fact that they show neither yellow nor vermilion nor bar. Any eosin son which shows one or more of these characters does so because his X chromosome has undergone crossing over, whereby a section (which may be that section carrying non-disjunction) has been replaced by a foreign section carrying these other genes but not non-disjunction.

The characters yellow, vermilion, and bar had been chosen because they would reveal crossing over at practically every point along the chromosomes. Yellow is at the zero end of the chromosome while bar is quite close to the other end. Vermilion is at the middle and would reveal the comparatively rare double crossing over. When double crossing over occurs, a section from the middle of the guarded chromosome would be replaced by a corresponding section from the middle of the other or guarding chromosome.

The daughters which show neither yellow nor vermilion nor bar will likewise have the eosin non-disjunction chromosome intact. The next step was then to mate such a daughter by the eosin male which had been selected. From their offspring the eosin sons which have non-disjunction can be again selected by the fact that they show neither yellow nor vermilion nor forked. The eosin daughters received non-disjunction from the father and also from the mother in all those cases where crossing over has not taken place. Therefore any eosin daughter which gives no yellow or vermilion or forked sons when mated to the selected eosin brother would give a stock homozygous for eosin and non-disjunction. From among several pairs of eosin daughters by eosin brothers one pair which gave only eosin offspring was chosen to supply the required stock.

To test the purity of the stock obtained in this way some of the eosin females were mated to wild males. Four of the five females gave exceptions but one did not (table 40).

TABLE 40

The offspring given by five eosin females of a special stock of non-disjunction when tested by wild males.

No.	Regular offspring		Exceptions		Percent of exceptions
	+♀	w^e♂	w^e♀	+♂	
1	62	50	—	4	3.5
1.1	73	64	—	2	1.4
2	19	10	—	3	9.4
4	62	36	4	3	6.6
Total	216	160	4	12	
3	73	62	—	—	—

From the next generation of the same stock, eosin females were again tested by wild males with the result that four of the nine females failed to give exceptions (table 41).

TABLE 41

The offspring given by nine females from the second generation of a special stock of non-disjunction when tested by wild males.

No.	Regular offspring		Exceptions		Percent of exceptions
	+♀	w^e♂	w^e♀	+♂	
78	65	78	—	1	.7
79	100	73	1	1	1.1
84	50	61	3	5	6.7
86	35	31	2	—	2.9
87	82	32	1	—	.9
Total	332	275	7	7	
80	78	90	—	—	—
82	111	54	—	—	—
83	52	60	—	—	—
85	88	64	—	—	—
Total	329	268	—	—	—

It is evident that the stock was not pure for non-disjunction. The method used was rigorous enough to prove that the failure to produce a stock homozygous for non-disjunction is due to the fact that there is no such thing in the X chromosome as a gene for secondary non-disjunction. The gap in the evidence left open in the last section is completely closed by this method, for the point midway between eosin and vermilion is guarded equally with the whole of the X chromosome.

(To be continued)

TEXT IS COMPLETE

PAGES 53 – 106 NOT PUBLISHED

NON-DISJUNCTION AS PROOF OF THE CHROMOSOME THEORY OF HEREDITY (concluded)

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CYTOLOGICAL PROOF OF THE OCCURRENCE OF XXY FEMALES

The breeding work presented in the last two sections has furnished data which show that the cause of secondary non-disjunction cannot be a gene carried by the X chromosome, while the same data are consistent with the assumption that a female which produces secondary exceptions does so because of the presence of an extra Y chromosome. Likewise the data from the tests of the constitution of the regular daughters, the regular sons, the exceptional daughters, and the exceptional sons, all lead to this same conclusion.

Accordingly, the prediction was made that cytological examination of the daughters of an exceptional female would demonstrate the presence of an extra chromosome in half of the daughters while the other half

would show only normal figures. This prediction has been completely verified.

The ovaries at the mid-pupal stage of development offer the best material for examination. Nearly a hundred pairs of ovaries were dissected from pupae of cultures the mother of which was an exceptional female. Eighteen of these gave oögonial metaphases which were clear enough to give a reliable count of the chromosomes.

Nine of the females showed figures like those published by Miss STEVENS (1908 a) in which the X chromosomes are a pair of straight rods. (See plate 1, figures 1-3, as well as the generalized group in figure 1, p. 3 of the first instalment).

The other nine females showed these two X chromosomes and in addition a chromosome which differed from both the X's in that it had the shape of a V with one arm shorter than the other. This chromosome was identified as the Y from the following considerations.

No figures which showed this extra chromosome were found by METZ (1914) when he examined the chromosomes of several wild stocks of *Drosophila ampelophila*. From the work of STEVENS (1908 a), METZ (1914) and myself (plate 1, figs. 1-3) there can be no doubt that the normal condition of the female is that shown in figure 1 (p. 3, first instalment.) The new type of figure which I found differs from the normal only by the addition of this chromosome. Fortunately, there are several good figures in each of four or five of the XXY females, and all the figures in any one female show the same condition.

The figures given by STEVENS, METZ, and myself, show that homologous chromosomes usually lie together as actual pairs. In the figures showing the extra chromosome, this chromosome is usually found in company with the two straight chromosomes so that it behaves as a homologue to them.

Very recently I have found several excellent spermatogonial figures in the testes of larval males; these show beyond question that the identification of the Y has been correct, for the Y has in these males the same characteristics as the supernumerary chromosome of the XXY females.

Breeding tests with sex-linked characters have shown that half the regular daughters produce exceptions to the inheritance of sex and sex-linked characters; parallel with this is the fact that half of the regular daughters possess this extra Y chromosome. Normal females do not possess this chromosome and do not produce exceptions, so that the exceptions must be produced by the daughters with the extra chromosome.

Recently over forty freshly hatched females which were first classi-

fied as exceptions were dissected and a cytological examination made of their chromosomes. In over a dozen of these individuals sufficiently clear figures were found to be sure of the number and character of the chromosomes. *In every case the exceptional female was found to be XXY.* This direct examination of the exceptions gives entirely conclusive proof that the cause of the production of secondary exceptions is the presence of the Y.

Miss STEVENS's (1908 a) work upon the male showed a pair of unequal chromosomes in place of the pair of equal straight rods of the female The longer of these two chromosomes seems to have the shape of a J in some of STEVENS's figures. The perpetuation of this longer chromosome in the male line can only be explained if these chromosomes have a causal connection with the differentiation of sex.

Of special interest is the condition shown in figures 20 to 24 (plate 1) which are from a single female with two X and two Y chromosomes, XXYY. This female was from a stock culture in which about half the females were expected to be XXY and half the males XYY. As we have seen, nearly half the eggs of an XXY female are XY, and thirty-three percent of the spermatozoa of an XYY male are XY. In the next generation therefore XXYY females should not be at all rare in such a stock. This female gave an unusual number of good figures, there being ten figures in which the identification of every chromosome is fairly certain.

This female has an additional value as evidence since the increase in the number of chromosomes is more striking, and since the occurrence of such a female gives indirect cytological proof of the occurrence of XYY males.

The ratio between XXY and XX daughters was much more easily determined by breeding tests than by cytological examination; accordingly only enough females were examined to prove that XXY females do actually exist. The proof of this point is beyond question. Also it chanced that the ratio of nine XXY to nine XX females was the equality expected from the breeding tests.

It will be noticed that often the figures show chromosomes split in preparation for the coming division. The difficulty in understanding the figures published by STEVENS disappears if it is assumed that in the male such a split in the long arm of the Y chromosomes appears relatively early while the short arm splits later. With this interpretation, practically every figure given by STEVENS falls into line with the evidence which the XXY females furnish, namely, that Y is the

Plate 1

The figures in this plate were drawn at table level; tube length 160 mm; Zeiss compensating ocular 12X; and Zeiss apochromatic 1.5 mm oil immersion objective, N.A. 1.30. The figures were then enlarged 2 ¼ diameters, and in reproduction were reduced in the ratio 3:2. The resulting magnification is 5,115 diameters.

Figures 1-3 are oögonial plates for wild females. Figures 2 and 3 are from the same cyst; figure 1 is from another individual. These figures are from freshly hatched mature flies; the rest of the figures are from pupae.

Figure 4 is a spermatogonial plate of a wild male (the extra granule is probably of no significance). I now have several good figures from the testes of larvae; four of these are diagrammatic in clearness, and show that the Y has the same character in the male as it has when transferred to the female.

Figures 5-19 are from XXY daughters of an exceptional mother. The plates are oögonial with the exception of 6 and 10 which are from other ovarian cells. Figures 5-10 are from one individual, as are 11-13, 14-16, 17, and 18-19. Figure 5 is of unusual clearness.

Figure 13 shows a typical late prophase in which the greatly elongated chromosomes are arranged about the periphery of the nucleus.

Figure 6 shows the X chromosomes just drawing into the equatorial plate; the outer ends are still curved in contact with the nuclear wall; the same is true of figure 8.

Figures 5, 7, 10-12, 13-16, and 19 are full metaphase groups.

Figure 9 shows a late metaphase group in which the chromosomes are already split; the same condition is seen in 4, 17, 18, and especially well in 20, 22, and 24. It is characteristic of this split that it begins at the free ends of the chromosomes and proceeds toward the spindle attachment; the separation at the point of attachment does not take place until the elongation of the cell.

Figures 20-24 are from an XXYY individual which was found in a stock mass culture in which half the parental flies were XXY females and half were XYY males.

In general the Y is the most sharply defined of all the chromosomes; this is seen especially well in early metaphases such as figure 6, or late metaphases such as figure 22.

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longer member of the XY pair, that it is attached sub-terminally, and has a J shape.

THE XX EGGS OF XXY FEMALES

Thus far in our analysis, the XX eggs of an XXY female have been considered mainly in their relation to the production of matroclinous daughters, but the method of origin of these eggs is interesting, if, as so far assumed, they are preceded by synapsis between an X chromosome and a supernumerary Y. In an ordinary XX female, synapsis takes place between X and X, and in an XXY female synapsis must be supposed to follow this same female type in 83.5 percent of cases. During or after synapsis of X with X, crossing over would have an opportunity to occur, and does occur, as will be shown in another section. While the frequency of this crossing over between the two synapsed X's of an XXY female is a little higher than normal the process must be essentially the same as that in an XX female.

But if synapsis in the XXY female should take the course that it follows in the male, where X has Y for its mate, *there would now be no chance of crossing over between the two X's, for one of them is in synapsis with another chromosome, the Y.* At the reduction division, Y and the X which conjugated with it, would pass to opposite poles, and the free X would go either with the Y or with the disjoined X. From those cases where the free X went with the disjoined X, XX eggs and Y eggs would result. The XX eggs should therefore always be *non-crossovers,* and this has been shown to be true.

It was noticed that when an XXY female carried eosin in one of her X chromosomes and vermilion in the other, the exceptional daughters were always like the mother in that they still carried eosin in one X and vermilion in the other. Linkage experiments have shown that about a third of the X eggs of an ordinary XX female are crossovers, that is, they carry both eosin and vermilion in the single X or conversely they carry neither. An experiment was made to find what percentage of XX eggs of an XXY female are crossovers, and the conclusion was reached that none of the XX eggs are crossovers.

If the XXY female is heterozygous for eosin, vermilion and forked instead of for eosin and vermilion only, a greater length of the X can be tested, and over half of the eggs instead of a third are expected to be crossovers under normal conditions. To obtain such females, wild type exceptional daughters (from table 37) were outcrossed to eosin vermilion forked males. The results are given in table 42.

TABLE 42

The offspring given by two wild type exceptional daughters from table 37(A) when outcrossed to eosin vermilion forked males.

No.	All daughters				Regular sons								Exceptions		Percent
	w^e v		w^e | v		w^e t v		w^e | t v		w^e t | v		w^e | t | v				
	w^ev +		w^e v		w^etv +		w^e tv		w^et v		w^ev t		w^evf ♂		
1030	48	48	18	20	48	53	10	20	3	3	—	1	6		4.2
1023	22	15	2	5	12	15	7	7	1	2	—	—	3		6.4
Total	70	63	20	25	60	68	17	27	4	5	—	1	9		

The wild type daughters of table 42 are heterozygous for eosin, vermilion and forked (regular daughters of which carry a Y chromosome, or they are rarely exceptions like their mother). Twelve of these daughters were mated to bar males, with the results shown in table 43.

TABLE 43

A. Regular wild type daughters from table 42 tested by bar males.

No.	Regular daughters	Regular sons										Exceptions				Percent of exceptions
		w^e v f		w^e | v f		w^e v | f		w^e | v | f				+ ♀		B′ ♂		
	B′	w^evf +		w^e vf		w^ev f		w^ef v								
1140	154	32	46	26	19	17	14	1	3			8		7		4.6
1148	74	16	23	4	7	2	4	—	1			4		3		5.1
1122	123	19	24	14	11	13	10	1	—			7		3		4.4
1135	113	25	27	15	20	19	8	4	4			12		5		6.7
1138	125	27	33	18	12	21	16	—	2			12		4		5.9
Total	589	119	153	77	69	72	52	6	10			43		22		5.4
1141	93	31	18	8	16	15	9	3	2			—		—		—
1147	143	29	43	10	16	7	10	4	3			—		—		—
1123	49	22	25	9	10	5	4	1	1			—		—		—
1133	74	26	19	7	6	6	5	1	2			—		—		—
1134	104	13	25	9	12	12	6	2	—			—		—		—
1139	43	12	11	5	5	6	8	—	—			—		—		—
Total	506	133	141	48	65	51	42	11	8			—		—		—

B. Exceptional wild type daughter from table 42 by a bar male.

No.	Regular daughters	Regular sons				Exceptions		Percent of exceptions
		w^e t v	w^e | | t v	w^e t | | v	w^e | | t | v			
	B′	w^etv +	w^e tv	w^et v	w^ev t	+ ♀	B′ ♂	
1146	79	24 37	7 12	2 2	— —	—	1	0.6

One of the daughters was herself an exception, as is shown by her offspring (table 43 *B*) which are like the offspring given by her mother. Of the eleven regular daughters five were XXY and six XX (table 43 *A*).

The exceptional daughters from the XXY cultures of table 43 *A*, furnish the material to be tested. Eight such wild type daughters were tested by bar males, and, as shown by their sons, they were all found (table 44) to be non-crossovers, each having eosin, vermilion and forked in one X and only unmutated genes in the homologous X, as their mothers had had.

TABLE 44

The results given by the exceptional wild type daughters from table 43 when tested by bar males.

No.	Regular daughters	Regular sons								Exceptions		Percent of exceptions
		w^e v f		w^e | | v f		w^e v | | f		w^e | | f | v				
	B′	w^evf +		w^e vf		w^ev f		w^ef v		+ ♀	B′ ♂	
1188	95	24	21	12	14	7	9	3	2	4	1	2.6
1259	125	33	37	15	10	6	8	2	4	8	5	5.1
1197	45	7	7	10	7	2	2	1	—	—	—	—
1186	138	41	53	22	14	12	15	6	—	8	7	4.8
1187	141	44	38	21	11	14	15	1	3	11	4	5.0
1215	115	29	24	12	12	12	10	—	—	8	10	7.8
1216	49	7	13	9	8	6	4	—	—	4	2	5.9
1220	83	20	17	16	11	9	8	1	1	3	7	5.7
Total	791	205	210	117	87	68	71	14	10	46	36	5.0

In subsequent generations twenty-nine more such exceptional daughters have been tested in the same way and all were found to be non-crossovers (table 45).

TABLE 45

The results given by the exceptional wild type daughters from table 44 when tested by bar males.

No.	Regular daughters	Regular sons								Exceptions		
		w^e v f		w^e | v f		w^e v | f		w^e f | v				
	B′	w^evf	+	w^e	vf	w^ev	f	w^ef	v	+♀	B′♂	Percent
1400	56	14	10	4	7	3	5	—	—	1	3	3.8
1353	38	8	10	2	4	2	6	—	2	3	—	4.0
1306	65	11	14	11	9	7	3	3	4	2	1	2.3
1332	92	23	23	10	14	6	8	7	1	3	—	1.6
1333	76	15	18	12	11	5	3	5	6	1	2	1.9
1354	18	5	4	1	3	1	—	1	—	—	—	—
1355	47	11	8	10	7	4	4	1	3	1	1	2.1
1334	125	29	39	11	20	17	11	2	1	14	13	9.6
1356	38	12	13	—	6	5	3	—	—	2	1	3.8
1304	99	25	14	10	8	17	7	3	—	5	4	4.7
1357	234	68	85	20	24	28	11	7	2	21	21	8.1
1418	83	16	25	9	15	3	9	4	1	1	1	1.2
1499	29	5	8	5	6	7	5	3	1	2	—	2.8
1500	9	2	1	2	3	1	2	—	—	—	1	4.8
1569	41	7	13	10	5	6	3	1	3	1	3	4.3
1571	71	13	12	12	8	7	8	1	3	3	8	7.5
1572	65	13	12	9	10	7	6	—	—	15	1	11.6
1573	47	11	17	6	6	1	2	1	—	7	—	7.1
1417	63	17	12	2	—	2	8	—	—	22	17	27.3
1503	92	18	28	4	10	8	8	3	—	4	9	7.1
1567	51	23	14	7	4	9	10	—	3	2	2	3.2
1689	56	16	10	5	9	2	2	—	1	3	1	3.8
1612	55	16	14	4	8	5	11	2	—	3	3	5.0
1613	77	15	23	12	10	9	8	2	—	2	4	3.7
1618	170	40	30	13	22	5	13	1	—	14	13	8.4
1624	39	16	9	6	1	4	4	1	—	2	1	3.6
1703	73	12	19	10	11	5	7	1	1	7	8	9.8
1714	188	36	43	28	15	17	17	4	1	10	11	5.7
1715	168	57	48	16	12	13	15	1	2	14	13	7.5(v♀1)
Total	2265	554	576	251	268	206	201	54	36	165	142	6.7

Not one of the thirty-seven exceptional daughters tested was a cross-over, although over twenty of them should have been crossovers if crossing over were of normal frequency. Several other exceptional daughters which were tested in other experiments, increase this evidence and show that crossing over does not occur in the formation of XX eggs. It will be demonstrated later that the XY and X egg of an

XXY female show no decrease in the amount of crossing over. No difference in the way the chromosomes pass to the poles at reduction can explain this difference in the amount of crossing over. The eggs destined to contain XX (or Y) must have begun to differ from those eggs destined to contain XY or X before the reduction division and before crossing over had taken place. This absence of crossing over between the two X's of an XX egg finds a ready explanation on the basis that the two X's were not in synapsis with one another, but that one of them was in heterosynapsis with the supernumerary Y of the XXY female so that crossing over between the two X's was impossible. On page 17 the percentage of cases in which XY synapsis occurs (16.5) was calculated from the percent of exceptions (4.3) given by XXY females.

It has been shown that the two X chromosomes which enter XX eggs are the same two chromosomes that combined in the production of the XXY mother. If these two original chromosomes are X and X′ the two final chromosomes are likewise X and X,′ *but not XX or X′ X′.* This fact proves that the XX-Y separation takes place at the division which in normal eggs would be the *reductional* division, and not at the equational division.

The evidence in this section proves that the ordinary type of non-disjunction is preceded by an XY synapsis and occurs at the reductional division.

SYNAPSIS IN XXY FEMALES

Females of the constitution XXY have been produced in the following three ways, namely, XX egg by Y sperm, XY egg by X sperm, and X egg by XY sperm. Irrespective of their origin, these XXY females have given the same percent of secondary exceptions. This means that the method of synapsis is not influenced by the origin of the chromosomes. Two chromosomes from the *same* parent synapse with each other as readily as though they were from different parents. Thus when both X's come from the mother, they synapse with each other in about 84 percent of cases, and crossing over takes place in about the normal amount. This is of interest in connection with the case of the tetraploid Primula, for as MULLER (1914) has shown, the data of GREGORY (1914) are in accord with the view that the four homologous chromosomes pair with each other, two by two, irrespective of whether they are from the same or from opposite parents.

That synapsis in an XXY female does not involve all three chromosomes at once, but is between two of them with the third chromosome left unsynapsed, is proved by the fact that the chromosomes of XX eggs are never crossovers, while the X's of the X and XY eggs are crossovers in about the usual percent. A difference between the paths followed by these two kinds of chromosomes originated before the stage at which crossing over became possible. If all three chromosomes synapsed together, there should not be this difference, for the X's which enter the XX egg should be crossovers in the same percentage as those which enter the X and XY eggs. Furthermore, it is difficult to see how two X's in synapsis with each other and at the same time with Y can cross over with each other without involving crossing over between the Y and one of the X's. There is no evidence that there is crossing over between X and Y in an XXY female. This leads us to suppose that in the male the lack of crossing over between X and Y is a property of Y and not entirely due to the general fact that there is no crossing over in the male of Drosophila between any chromosomes.

CROSSING OVER IN XXY FEMALES

Besides the production of XX eggs both of whose X's are non-crossovers, there is another consequence of XY synapsis which may be examined. After heterosynapsis Y and the synapsed X disjoin and the free X goes with the Y in half the cases. The resulting XY and X eggs must also be *non-crossovers* since there has been no XX synapsis which would give an opportunity for crossing over to occur. When these eggs are fertilized, they give rise only to regular offspring and should *increase the non-crossover classes of the regular offspring*. Because of this added source of non-crossovers the percentages of crossing over should be *less* than those shown by sister XX cultures. If the free X goes with Y as often as with the disjoined X then the number of these added non-crossover X and XY eggs will be equal to the number of XX and Y eggs. The number of XX and Y eggs is equal to twice the number of surviving exceptions (the XXX and YY zygotes die), so that the number of non-crossovers added from heterosynapsis can be found by doubling the number of observed exceptions. A comparison of the percentages of crossing over shown by XXY and XX cultures should be interesting, and the regular sons of many of the experiments furnishing such data, are summarized in the following tables.

TABLE 45A

A summary of the sons in XXY cultures where three genes were involved.

Genes	—	| —	— |	| — |	Total	Exceptional sons	Coincidence	Data from tables
yw^{e}v	491	7	172	2	672	97	86	25
w^{e}tv	1693	606	132	5	2436	65	15	37, 42, 43, 47
w^{e}vf	1890	915	704	142	3651	202	59	43, 44, 45, 63

The first of these tables gives those cases in which crossing over between more than two genes is involved. The data of this table are also included in the following table, which gives the totals for each separate crossover value.

TABLE 45B

A summary of all crossover data from XXY cultures.

Genes	Total sons	Crossovers	Crossover value	Exceptional sons	Corrected value	Data from tables
yw^e	672	9	1.3	97	2.0	25
yv	672	179	26.7	97	37.4	25
w^{e}t	2436	601	24.7	65	26.0	37, 42, 43, 47
w^{e}v	13,014	3937	30.7	580	33.7	9, 12, 23, 25, 35A, 36, 37(*A*), 37(*C*), 42, 43*A*, 43*B*, 44, 45, 47, 56, 63, 77, 86
w^{e}f	3651	1619	44.4	202	49.8	43, 44, 45, 63
w^{e}B′	257	114	44.3	21	53.0	3, 79
tv	2436	137	5.6	65	5.9	37, 42, 43, 47
vf	3651	846	23.2	202	26.0	43, 44, 45, 63

Before discussing these results it is well to summarize the crossing over results given by the XX females. In one case four genes, eosin, vermilion, sable and forked, were run together, and gave the following data.

TABLE 45C

A summary of the sons of XX cultures involving four genes, from tables 34 and 66.

Genes	—	| —	— |	| —	— | |	| — |	| | —	| — | |	| | — |
w^{e}vsf	2708	1213	417	543	55	116	12	0

The two following three-locus cases occurred.

TABLE 45D

A summary of the sons of XX cultures where three genes were involved.

Genes					Total	Coincidence	Tables
$w^e tv$	1887	627	139	7	2600	19.7	37
$w^e vf$	623	305	223	47	1198	59.4	43, 63

The data from both these tables combined with the other data upon two-locus experiments give the following summary for the offspring of XX cultures.

TABLE 45E

A summary of all crossover data from XX cultures.

Genes	Total	Crossovers	Crossover value	Data from tables
$w^e t$	2600	634	24.4	37
$w^e v$	15,177	4479	29.5	9, 12, 23, 28, 34, 37, 43, 56, 63, 66, 77
$w^e s$	5064	1758	34.7	34, 66
$w^e f$	6262	2701	43.1	34, 43, 63, 66
$w^e B'$	1699	744	43.6	10, 29, 30, 57, 79
tv	2600	146	5.6	37
vs	5064	484	9.6	34, 66
vf	6262	1401	22.4	34, 43, 63, 66
vB′	311	67	21.5	57

On comparing the summary of the results for the XXY cultures with this summary of the results for the XX cultures it is seen that not all of the crossover values occur in both. Those cases in which data of both sorts are present are compared in the following table.

TABLE 45F

A comparison of the crossover values from XX and XXY cultures.

Genes	XX cultures		XXY cultures		Increase	Percentage increase
	Total	Crossover value	Total	Corrected value		
$w^e t$	2600	24.4	2436	26.0	1.6	6.6
$w^e v$	15,177	29.5	12,817	33.7	4.2	14.2
$w^e f$	6262	43.1	3651	49.8	6.7	15.5
$w^e B'$	1699	43.6	257	53.0	9.4	21.6
tv	2600	5.6	2436	5.9	0.3	4.6
vf	6262	22.4	3651	26.0	4.4	19.6

At once the rather startling fact becomes apparent that in every case the percent of crossing over given by the XXY females has risen slightly. The mean increase in the corrected values is 13.5 percent over the values given by the XX cultures. This increase is in some manner due to the presence of the Y in the XXY females, though the mechanism whereby the Y produces such an increase is unknown. The increase does not seem to be confined to one section of the chromosome but seems to be practically uniform throughout the length of the X.

It is possible that some of the assumptions made in the analysis are unwarranted, and that the increase is accordingly only an apparent one. For example, if when X and Y disjoin the free X goes with the disjoined X much more often than with the Y, then only a few non-crossovers would be added to the regular offspring. Some work now under way makes it seem probable that the change in the amount of crossing over is a real one and that it is not necessary to suppose that the assortment at reduction is preferential.

XXX ZYGOTES

By primary non-disjunction in an XX female, and by secondary non-disjunction in an XXY female, XX eggs are produced. We have studied the matroclinous daughters which originate from the fertilization of these eggs by Y sperm; and we have assumed that the equally numerous XXX zygotes produced by the fertilization of XX eggs by X sperm are unable to live. On *a priori* grounds one would expect that XXX zygotes would survive as females. These females might be classified either with the exceptional or with the regular daughters, according to whether the two recessives or the dominant allelomorph produced the greater effect upon the character. More probably the character would be intermediate between the dominant and the recessive, since even in a normal heterozygote there is usually discernible some effect of the recessive. A watch has been kept for such intermediates among the daughters of XXY females, but none have been found. Inspection thus shows that the XXX zygotes do not survive, or else are similar in appearance to the exceptional or to the regular daughters. That they are not among the exceptional daughters is proved by the fact that this class is not more numerous than the exceptional male class, and by the fact that over three hundred of these exceptional daughters have been bred and were all of one type. Likewise about two hundred of the regular daughters have been bred, and none of them gave the peculiar results that an XXX female would be expected to give, namely, a three-female-

to-one-male sex ratio, a ratio of two recessives to one dominant among the sons, a large number of exceptional daughters, and one third of these exceptional daughters of the recessive type. Thus, for example, an XXX female carrying recessive white in two of the X's and the unmutated dominant wild type gene in the other X (w w +) would be wild type in appearance. Bred to a bar male the offspring should be:

Regular daughters	Regular sons	Exceptional daughters	Exceptional sons
6 B′	2w, 1 +	2 +, 1 w	0 B′

If it is still to be supposed that XXX females survive, it must be assumed that they are sterile, since none gave aberrant results among the two hundred regular daughters tested. Only eight or nine would be expected among two hundred regular daughters, and thus the occasionally sterile individual would not seem unusual. While the probability is that XXX zygotes die, this evidence does not yet establish it as a fact.[8]

YY AND YO ZYGOTES

By secondary non-disjunction an XXY female produces as many Y as XX eggs. These Y eggs when fertilized by X sperm give patroclinous sons, but when fertilized by Y sperm give YY zygotes which are unable to live. Such zygotes could not be females for it requires two X chromosomes to develop a female. Every male in a culture shows the sex-linked characters of the mother (regular sons) or of the father (exceptional sons); YY individuals can not be among these males since a YY individual could show no sex-linked characters whatever. By primary non-disjunction eggs with no sex chromosome arise, and these fertilized by Y sperm give YO zygotes which die, as do those with YY.

EQUATIONAL NON-DISJUNCTION

It may now be shown that there is another type of exception which does not preclude XX synapsis, and which occurs at an equational division.

Very rarely a female which is heterozygous for a recessive sex-linked gene produces an exceptional daughter which is pure recessive. Thus a wild type XXY female carrying eosin in one X and vermilion in the other produced an eosin exceptional daughter (culture 600, table 9).

[8] Some work on high non-disjunction now under way proves definitely that XXX zygotes die.

This eosin exception was herself heterozygous for vermilion, as her offspring showed when she was mated by a tan vermilion male (table 46).

TABLE 46

The offspring given by an eosin equational exception from table 9 when tested by a tan vermilion male.

No.	Regular offspring				Exceptions		Percent
	v ♀	+ ♀	w^ev ♂	w^e ♂	w^e ♀	tv ♂	
633	41	52	34	36	4	2	3.5

The presence of the vermilion and the fact that exceptions were produced are both strong indications that no error, such as non-virginity or contamination, occurred. In the case of certain other like exceptions which appeared later there is complete proof of the genuineness of this type of exceptions.

Although in the mother of the eosin exception, eosin was carried in one X and vermilion in the other, in the daughter *one of the X's carried both eosin and vermilion.* There must, then, have been crossing over, preceded by an XX synapsis. The other X of the eosin daughter carried only eosin and therefore was a non-crossover chromosome. The very remarkable case is thus presented of an exceptional daughter, one of whose X chromosomes has undergone crossing over while the other has not!

The chiasmatype hypothesis of crossing over offers a very simple ex-

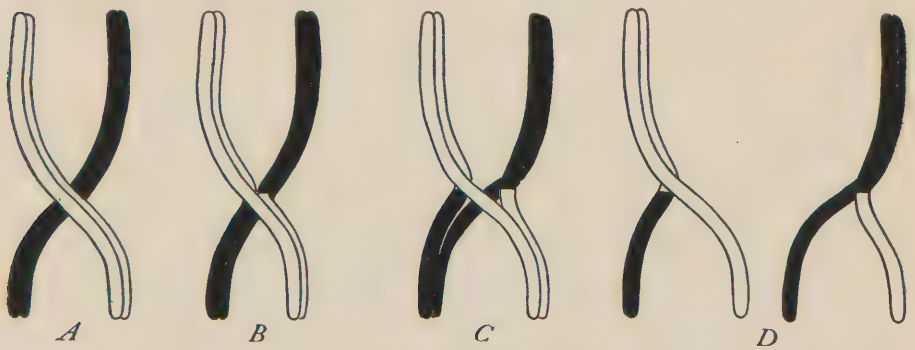


FIGURE 9.—Four stages in crossing over, according to the chiasmatype theory of JANSSENS. The maternal and paternal chromosomes come together, twist about each other, split lengthwise so that four strands result (*A*), and crossing over takes place between only two of the strands (*B*). The reduction division (*C* and *D*) segregates two strands to each cell. (After MORGAN, STURTEVANT, MULLER, and BRIDGES.)

planation of exceptions of this type. In certain known cases, the two X's may come together, twist about each other, and then each split lengthwise, so that four strands are formed. It has been assumed by JANSSENS (1909) that at this stage, where the strands lie in contact there may be crossing over between two without crossing over between the other two. As the strands draw apart each cell should thus receive a crossover and a non-crossover chromosome. If non-disjunction occurred at this stage XX eggs would be formed in which one chromosome is a crossover and the other a non-crossover. Such an egg would give rise to an exceptional daughter of the type actually found.

It is impossible to obtain exceptions of this type from an XX or XXY oöcyte unless the crossing over has taken place at a four strand stage. Therefore the proof that these exceptions have arisen from such oöcytes will at the same time be proof that crossing over takes place during a four strand stage, to which process JANSSENS has given the name chiasmatype.

A few of the offspring of the eosin exceptional female were tested, although there seemed no reason to suppose that they would be in any way different from ordinary XX and XXY flies. One of the wild type daughters tested by yellow white males gave only offspring expected from a regular XXY daughter, as shown by table 47.

TABLE 47

The offspring given by a wild type regular daughter from table 46 when tested by a yellow white male.

No.	Daughters		Regular sons								Exceptions	Percent.
	w-w^e	+	w^e	tv	w^etv	+	w^ev	+	w^et	v	yw ♂	
771	59	80	33	35	24	28	2	5	—	—	4	3.1

Three of the eosin exceptional daughters were tested and they proved to be duplicates of the mother; that is, they were heterozygous for vermilion, as expected from their origin through secondary reductional non-disjunction (tables 48, 49 and 50).

TABLE 48

The offspring given by an eosin reduction-exceptional daughter from table 46 when mated by a yellow male.

No.	Regular offspring			Exceptions		Percent
	+ ♀	$w^e v$ ♂	w^e ♂	w^e ♀	y ♂	
750	42	20	26	—	2	2.2

TABLE 49

The offspring given by an eosin reduction-exceptional daughter from table 46 when mated by a yellow white male.

No.	Regular offspring			Exceptions		Percent
	w-w^e ♀	$w^e v$ ♂	w^e ♂	w^e ♀	yw ♀	
800	126	50	67	1	4	2.0

TABLE 50

The offspring given by an eosin reduction-exceptional daughter from table 46 when mated by a vermilion male.

No.	Regular offspring				Exceptions			
	v ♀	+ ♀	$w^e v$ ♂	w^e ♂	w^e ♀	v ♂	Percent	$w^e v$ ♀
712	47	49	51	52	8	11	8.7	1

One of the three eosin daughters (tested by vermilion males, table 50) gave an eosin vermilion exceptional female which is a second case of equational non-disjunction. This immediately suggests that the tendency to produce equational exceptions may be inherited. Rather extensive tests of the offspring were accordingly made.

One of the eosin reductional exceptions tested by pink males gave no equational exceptions (table 51). Pink is an autosomal eye-color (third chromosome) and was used because its presence (heterozygous) in an equational exception would prove beyond question that the intended cross had been made and that no error was responsible for the so-called equational exceptions.

TABLE 51

The offspring given by an eosin reduction-exceptional daughter from table 50 when mated to pink males.

No.	Regular offspring			Exceptions		
	+ ♀	$w^e v$ ♂	w^e ♂	w^e ♀	+ ♂	Percent
772	152	54	62	3	2	1.8

Likewise, four of the regular wild type daughters of table 50 were tested by pink males, but none of these gave equational exceptions (table 52).

TABLE 52

The offspring given by four wild type regular daughters from table 50 when mated by pink males.

No.	All females	All males	Equational female
773	161	166	—
774	162	185	—
775	64	39	—
776	157	170	—
Total	544	560	—

Two of the vermilion regular daughters tested by pink males gave no equational exceptions (table 53).

TABLE 53

The offspring given by two vermilion regular daughters from table 50 when mated by pink males.

No.	Regular offspring			Exceptions		
	+ ♀	$w^e v$ ♂	v ♂	v ♀	+ ♂	Percent
778	144	84	82	1	1	.6
777	156	86	73	—	—	—

Four more vermilion regular daughters tested by forked or by bar males gave no equational exceptions, as is shown in tables 54 and 55.

TABLE 54

The offspring given by a vermilion regular daughter from table 50 when mated by forked males.

No.	Regular offspring			Exceptions		
	+ ♀	w^ev ♂	v ♂	v ♀	f ♂	Percent
768	132	64	77	—	—	—

TABLE 55

The offspring given by three vermilion regular daughters from table 50 when mated by bar males.

No.	Regular offspring			Exceptions		
	B′ ♀	w^ev ♂	v ♂	v ♀	B′ ♂	Percent
815	175	64	79	4	5	2.8
817	160	70	92	1	3	1.2
Total	335	134	171	5	8	—
816	140	81	87	—	—	—

Finally three of the wild type regular daughters were tested by bar males, with the result that one gave a vermilion daughter which is a third case of equational exception (table 56).

TABLE 56

The offspring given by three wild type regular daughters from table 50 when tested by bar males.

No.	Regular daughters	Regular sons				Exceptions			
		w^e / v		w^e | v					
	B′	w^e	v	w^ev	+	+ ♀	B′ ♂	Percent	v ♀
819	143	37	39	18	29	1	4	1.8	—
818	141	58	50	29	17	—	—	—	—
820	171	71	56	33	33	—	—	—	1
Total	312	129	106	62	50	—	—	—	—

In the culture in which the vermilion exception occurred there were no secondary reductional exceptions, the vermilion equational female being the only exception. This absence of other exceptions is not a complete proof that the mother was not XXY; but eight of the regular bar daughters, tested by miniature males (table 57), all failed to give secondary exceptions, which proves conclusively that the mother of the vermilion equational females was XX and that the non-disjunction was primary. It is not remarkable that this third case of equational non-disjunction should have been a primary exception, produced by an XX mother, for the presence of an extra Y cannot explain this type of non-disjunction.

TABLE 57

The offspring given by eight bar regular daughters from table 56 when mated by miniature males.

No.	All daughters	Regular sons				Exceptions
		v / B′		v | B′		
		v	B′	vB′	+	m ♂
976	55	17	23	7	8	—
977	31	17	10	4	1	—
979	47	20	32	5	4	—
1016	115	34	20	6	6	—
1018	129	36	35	15	11	—
Total	377	124	120	37	30	—
	♀ ♀	w^e	B′	w^eB	+	
1017	154	32	33	30	39	—
978	124	124				—
1015	91	106				1 (sterile)

A fourth case of equational exception was an eosin daughter produced by a wild type female heterozygous ("repulsion") for eosin and vermilion (culture 829, table 28). This case also, as has been already shown by the evidence of table 29, was due to primary non-disjunction.

The vermilion equational female recorded in table 56 was outcrossed to eosin males, and showed by her offspring that she was heterozygous for eosin (table 58).

TABLE 58

The offspring given by a vermilion equational daughter from table 56 when tested by an eosin male.

No.	Regular offspring				Exceptions	
	w° ♀	+ ♀	w^e v ♂	v ♂	v ♀	w^e ♂
938	18	26	24	27	—	—

This exception, like the first, possessed one crossover and one non-crossover chromosome, and suggests the same explanation.

Three of the wild type regular daughters (from table 58) were outcrossed to arc speck males but none of them gave equational exceptions (table 59). Arc and speck are second-chromosome characters which were used to check the result in the same manner as pink was used in the first instance.

TABLE 59

The offspring given by three wild type regular daughters from table 58 when mated by arc speck males.

No.	Females	Males	Equational females
1076	71	73	—
1077	110	94	—
1078	104	91	—
Total	285	258	—

Tests of this same type were applied to a fifth and a sixth case of equational daughters which arose in an unrelated experiment (see pedigree, page 14). Exactly as in the first case, eosin exceptional daughters heterozygous for vermilion arose from mothers which carried eosin in one X and vermilion in the other (cultures 785 and 834, table 23). Each of these eosin daughters was tested by vermilion males and the offspring (table 60) show that they were heterozygous for vermilion.

Several of the wild type daughters from table 60, mated to arc speck males, gave no equational exceptions (table 61).

TABLE 60

The offspring given by two eosin equational daughters from table 23 when mated to vermilion males.

No.	Regular offspring				Exceptions		
	v ♀	+ ♀	w^ev ♂	v ♂	w^e ♀	v ♂	Percent
937	47	58	56	56	2	4	2.7
936	63	57	66	55	5	3	3.2
Total	110	115	122	111	7	7	

TABLE 61

The offspring given by eight wild type regular daughters from table 60 when mated to arc speck males.

No.	Females	Males	Equational females
1072	124	55	—
1073	182	154	—
1074	21	33	—
1075	111	110	—
Total	438	352	—
1068	106	71	—
1069	100	132	—
1070	49	32	—
1071	111	104	—
Total	366	339	—

The second equational female, an eosin vermilion daughter, recorded in table 50, was outcrossed to forked males, and proved to be an XXY female as shown in table 62.

TABLE 62

The offspring given by an eosin vermilion equational female from table 50 when mated to forked males.

No.	Regular offspring		Exceptions		
	+ ♀	w^ev ♂	w^ev ♀	+ ♂	Percent
769	132	111	5	3	3.2

Seven of the wild type regular daughters of table 62 were outcrossed to white bar males. One of these (table 63) gave an eosin vermilion daughter, the seventh equational exception.

TABLE 63

The offspring given by seven wild type regular daughters from table 62 when mated to white bar males.

No.	Regular daughters	Regular sons								Exceptions		
		$\frac{w^e\ v}{\ \ f}$		$\frac{w^e\ \|\ f}{\|\ v}$		$\frac{w^e\ v\ \|\ f}{\ \ \|}$		$\frac{w^e\ \|\ \|}{\|\ v\ \|\ f}$				
		$w^e v$	f	$w^e f$	v	$w^e vf$	+	w^e	vf	+♀	wB′♂	Percent
887	102	24	16	13	9	9	11	1	9	1	2	1.5 (w^ev♀ 1)
923	67	18	15	5	11	9	5	—	2	1	—	.8
Total	169	42	31	18	20	18	16	1	11	2	2	—
888	105	22	29	12	16	8	10	—	1	—	—	—
889	63	20	18	8	5	4	4	3	1	—	—	—
890	264	69	58	24	46	24	32	10	4	—	—	—
892	160	39	31	13	22	10	10	2	3	—	—	—
922	136	28	35	23	23	16	12	—	4	—	—	—
Total	728	176	171	80	112	62	68	15	13	—	—	—

The eosin vermilion equational exception from table 63 was mated to sable forked males and proved to be heterozygous for forked (table 64). Here again the eosin vermilion forked X was a crossover and the eosin vermilion X a non-crossover.

TABLE 64

The offspring given by an eosin vermilion equational daughter from table 63 when mated to a sable forked male.

No.	Regular offspring				Exceptions		
	f♀	+♀	w^evf♂	w^ev♂	w^ev♀	sf♂	Percent
1044	51	43	48	48	6	2	4.

Two of the eosin vermilion exceptional daughters from table 64 gave regular offspring and reductional exceptions, but no equational exceptions (table 65).

TABLE 65

The offspring given by two eosin vermilion reductional exceptions from table 64 when mated to sable forked males.

No.	Regular offspring				Exceptions		
	f ♀	+ ♀	w^evf ♂	w^ev ♂	w^ev ♀	sf ♂	Percent
1143	85	90	73	69	8	9	5.7
1156	63	56	50	60	4	6	4.2
Total	148	146	123	129	12	15	

Five of the wild type regular daughters from table 64 tested by bar males gave no exceptions (table 66).

TABLE 66

The offspring given by five wild type regular daughters from table 64 when mated to bar males.

No.	Regular daughters	Regular sons														Exceptions	
	B′	w^ev	sf	w^esf	v	w^evsf	+	w^evf	s	w^e	vsf	w^es	vf	w^evs	f	w^ef	vs	+♀	B′♂
1154	40	12	13	9	6	—	2	—	6	—	—	1	—	—	—	—	—	—	—
1155	190	36	37	13	36	12	11	10	7	1	1	2	2	—	1	—	—	—	—
1198	139	30	26	15	15	5	5	5	5	—	—	1	1	—	—	—	—	—	—
1212	78	17	16	9	6	3	1	6	2	—	—	1	1	—	—	—	—	—	—
1233	196	58	73	14	20	4	4	10	13	2	—	3	—	—	—	—	—	—	—
Total	653	153	165	60	63	24	23	31	33	3	1	8	4	—	1	—	—	—	—

In an experiment which is reported in the following section, a wild type XXY female which carried eosin in one X and whose other X was unmutated, produced an eosin exceptional daughter (table 77, culture 1221). Since there were no control characters nothing was done with the exception.

In a sister culture (number 1217, table 77) an XXY wild type female which carried eosin and vermilion in one X and neither in the other, produced two eosin and two vermilion equational daughters. Each of these four exceptions contained one crossover and one non-crossover chromosome, as the tests in table 67 show.

TABLE 67

The offspring given by two eosin and two vermilion equational daughters from table 77 when outcrossed to sable forked males.

A. Offspring from the two eosin daughters.

No.	Regular offspring			Exceptions		
	+ ♀	$w^e v$ ♂	w^e ♂	w^e ♀	sf ♂	Percent
1352	94	35	45	1	3	2.2
1403	106	66	51	6	2	3.5
Total	200	101	96	7	5	

B. Offspring from the two vermilion daughters.

No.	Regular offspring			Exceptions		
	+ ♀	$w^e v$ ♂	w^e ♂	w^e ♀	sf ♂	Percent
1408	206	104	92	4	7	2.7 ($w^e v$ ♀ 1)
1566	26	10	14	1	1	3.8
Total	200	114	106	5	8	

One of the four produced a further equational exception, which was an eosin vermilion daughter (culture 1408, table 67).

A large number of the wild type regular daughters from these four cultures of table 67 were mated to black males (table 68). One which carried eosin and vermilion in one X and sable and forked in the other, produced an eosin sable equational daughter (culture 1553).

TABLE 68

The offspring given by the regular wild type daughters from table 67 *when outcrossed to black males.*

A. Offspring from daughters from culture 1352.

No.	Females	Males	Equational exceptions
1527	29	51	—
1528	98	105	—
1529	137	149	—
1530	75	54	—
1531	101	112	—
1533	37	37	—
1535	132	114	—
1536	78	61	—
1537	100	93	—
Total	709	776	—

B. Offspring from culture 1403.

1547	107	149	—
1548	75	83	—
1551	96	97	—
Total	278	329	—

C. Offspring from culture 1408.

1552	69	62	—
1553	68	65	1 (w^es ♀)
1578	174	141	—
1580	94	99	—
1581	145	154	—
1582	113	107	—
1584	117	104	—
1585	138	107	—
1586	126	122	—
Total	1044	961	—

This exception in culture 1553 was tested by black males (table 69).

TABLE 69

The offspring given by the eosin sable equational exceptional daughter from table 68 when tested by black males.

No.	Regular offspring			Exceptions		
	Black ♀	+ ♀	$w^e s$ ♂	$w^e s$ ♀	+ ♂	Percent
1669	5	5	5	1	—	6.3

The fact that half the daughters were black is proof that no error has occurred. Both of the X's were crossovers between eosin and vermilion and at least one was a crossover between sable and forked, that is, a double crossover. Whether the other X was also a double crossover or not is uncertain because the sons were too few in number (5) to show that the mother was not heterozygous for forked.

Another equational exception, the fifteenth case, was a yellow white daughter produced by a mother carrying yellow and white in one X and eosin and vermilion in the other (table 78, culture 1285). This female died by accident so that it is not known whether she was heterozygous for vermilion or not.

In culture 1424, table 34, an XX wild type female carrying eosin and vermilion in one X and sable and forked in the other produced by primary non-disjunction a wild type female and an eosin vermilion female. The eosin vermilion female was sterile, an unexplained circumstance. The wild type female died by accident.

In table 25, culture 1657, a wild type XXY female carrying yellow, eosin and vermilion in one X and no mutant genes in the other, gave a yellow eosin daughter which the test showed was heterozygous for vermilion (table 70).

TABLE 70

The offspring given by the yellow eosin equational daughter from table 25 when mated to bar males.

No.	Regular offspring			Exceptions		
	B′ ♀	$yw^e v$ ♂	yw^e ♂	yw^e ♀	B′ ♂	Percent
1727	141	60	47	13	11	8.8

In table 45, culture 1715, a wild type XXY female carrying eosin, vermilion and forked in one X and no mutant genes in the other, produced a vermilion daughter which was heterozygous for both eosin and forked. One X must therefore have been a double crossover and the other a non-crossover (table 71).

TABLE 71

The offspring given by the vermilion equational daughter from table 45 when mated to sable males.

No.	Regular offspring					Exceptions		
	+ ♀	w^evf ♂	v ♂	w^ev ♂	vf ♂	v ♀	s ♂	Percent
1736	91	20	31	19	21	2	4	3.2

There have been eighteen instances of equational exceptions. In thirteen of these cases, crossing over is known to have occurred, and this is *in every case where evidence upon this point was obtainable.* Again, of these thirteen cases which involved crossing over, *twelve were crossovers in only one chromosome and were non-crossovers in the other.* The thirteenth case was a double crossover in one chromosome and at least a single crossover in the other. Although fifteen of the instances occurred in XXY females, three occurred in females known to be simply XX, and it is thus evident that equational non-disjunction is not caused by the presence of a Y. The descendants of equational exceptions seem to have a greater tendency to produce further equational exceptions, though no basis for this tendency has been found.

As previously explained, all these exceptions are easily accounted for in the following way: XX synapsis took place; each X split so that a four strand stage occurred; crossing over took place between two only of these strands, one from each X; the reduction division separated the paternal X from the maternal X, each cell receiving a non-crossover and at the same time a crossover strand; at the next division these two strands ordinarily enter different cells, but by an occasional non-disjunction these two strands do not separate from each other at the equational division and consequently enter the same nucleus. In the case of an XX female the presence of the Y might favor the process by entering the other cell so that one cell receives two X chromosomes and the other two Y's. Equational non-disjunction thus enables us to examine at leisure the products of reduction.

It is impossible that a non-crossover and a crossover chromosome

come from a cell in which only two strands are present. Therefore the proof that these exceptions arise from XX (or XXY) oöcytes would at the same time prove that crossing over took place in this manner at a four strand stage.

If, however, the oöcyte contained three X chromosomes, synapsis and crossing over might occur between two of them and the equational split appear after the crossing over had been accomplished. At the reduction division the two synapsed X's (which would also be crossovers in a certain percent of cases) would disjoin and pass to separate poles, while the free X, which would always be a non-crossover, would go with one or the other according to chance. In those cases in which crossing over has occurred and a crossover and the free non-crossover X have remained in the egg after reduction, the equational division would make no quantitative change. These eggs fertilized by Y sperm would give exceptions having all the characteristics of those just described.

But none of these equational exceptions came from XXX mothers; for it is quite certain that XXX females do not live. It is possible, however, that a small group of XXX cells in an XX female might live if such cells were produced. Let us suppose that in a germ-tract division the two daughter chromosomes from one X were late in separating from each other, while the other X divided normally. Then both these X's might become caught in one cell as in other cases of primary non-disjunction. One cell from such a division would be X and the other X X′ X′ in composition, having two maternal (or paternal) X's and one of the contrary type. This X X′ X′ cell might give rise to a group of such cells in the germ-tract and these might cause the production of several equational exceptions in a single culture, as in culture 1217, table 77.

The twelve cases in which one of the X's was a non-crossover and the other a crossover chromosome are equally well explained on either the chiasmatype or the X X′ X′ view. The thirteenth case in which one X was a double crossover and the other X probably also a double crossover could be explained on either view as a case of primary non-disjunction at the second maturation division.

Yet if an equational exception should arise such that one of its X's were a double crossover and the other a single crossover between two of the same genes involved in the double crossover, then the X X′ X′ view could not be applied, for one strand cannot cross over at the same point with each of two other strands. Of the two exceptions which might

have answered this question, one did not give enough offspring to settle its nature and the other could have arisen by either method. The evidence in hand thus allows us no conclusion as to whether crossing over takes place at a two or four strand stage; but equational non-disjunction offers the possibility of answering this question definitely.[9]

SOMATIC NON-DISJUNCTION AND GYNANDROMORPHISM

If the same sort of primary non-disjunction which has been assumed to give rise to X X′ X′ cells in an XX female, should take place at a cleavage stage, gynandromorphs and mosaics would result. One might expect at an early cleavage division, particularly the first, a relatively large number of X—X X′ X′ divisions, for the greatly condensed chromosomes introduced by the sperm do not for some time attain the state or the appearance of those of the egg nucleus. If the paternal X of a female were slower than the maternal in preparing for division, it might lag upon the spindle so that both daughter X's would become included in the same cell. The portion of the fly which comes from the X cell should be male and should show the sex-linked characters of the mother. Such a process may be the explanation of the large number of lateral gynandromorphs of Drosophila. When the X—X X′ X′ division occurs at a later cleavage stage we may have mosaics, as for example, a red female with a patch of white facets in the eye.

HIGH NON-DISJUNCTION

The mean of the percentages of exceptions given by all the XXY cultures is 4.3 percent and the mode is at about 2.3 percent. Occasionally rather high percentages occur. For example, one of three regular white-eosin daughters from culture 800 gave nearly 14 percent of exceptions, while a sister gave 8 percent (table 73).

[9] The conclusive evidence that crossing over does take place at a four strand stage according to the chiasmatype hypothesis came Dec. 16, 1915, with the discovery of an equational female one of whose X chromosomes had undergone double crossing over while the other had undergone single crossing over at the same level (between the same two genes) at which the first crossover of the double had occurred. The mother of this exception was an XXY female of the constitution $\frac{v\ \ f}{sg}$; the two recessive characters vermilion and forked were in one X, and the two recessive characters, sable and garnet, were in the other (for garnet see p. 151). The equational exception was of the constitution $\frac{v\ \ sg}{\ }$; the chromosomes represented by the space below the line (unmutated genes only) is a double crossover, and the chromosome represented above the line is a single crossover which had taken place between vermilion and sable, that is, in the same region in which the first single of the double had occurred.

TABLE 73

The offspring given by three white-eosin regular daughters from table 49 when outcrossed to wild males.

No.	Regular offspring		Exceptions		
	+ ♀	♂♂	w-w^e ♀	+ ♂	Percent
931	80	112	1	1	1.
932	77	74	11	13	13.7
933	113	112	11	8	7.8
Total	270	298	23	22	

From each of these cultures two exceptional daughters were tested. Each gave percentages somewhat higher than normal (table 74).

TABLE 74

The offspring given by four white-eosin exceptional daughters from table 73 when outcrossed to bar or wild males.

A. Two daughters from culture 932 mated to wild males.

No.	Regular offspring		Exceptions		Percent
	+ ♀	♂♂	w-w^e ♀	+ ♂	
1079	158	122	14	14	9.4
1080	157	159	6	10	4.8
Total	315	281	20	24	

B. Two daughters from culture 933 mated to bar males.

1039	129	123	14	6	7.4
1040	127	121	4	9	5.
Total	256	244	18	15	

Three exceptional daughters from culture 1039 (table 74) gave only low percentages of exceptions (table 75).

TABLE 75

The offspring given by three white-eosin exceptional daughters from table 74 when outcrossed to wild males.

No.	Regular offspring		Exceptions		
	+ ♀	♂♂	w-w^e ♀	+ ♂	Percent
1151	92	92	5	1	3.2
1152	83	95	5	2	3.8
1153	97	77	1	1	1.1
Total	272	264	11	4	

Two similar exceptional daughters from culture 1079 (table 74), gave high percentages of exceptions (table 76).

TABLE 76

The offspring given by two white-eosin exceptional daughters from table 74 when mated to bar males.

No.	Regular offspring		Exceptions		
	B′ ♀	♂♂	w-w^e ♀	B′ ♂	Percent
1184	110	80	11	9	10.0
1202	5	13	15	14	62.0
Total	115	93	26	23	

Up to this point none of the cultures have been so aberrant that they do not fall into the normal curve.

However, one of the cultures of table 76 produced *more exceptions than regular offspring, and this culture seems to belong to a different category of non-disjunction.*

Twelve of the regular daughters from culture 1079 were tested and one (culture 1164, table 77) likewise gave a remarkably high percentage of exceptions.

TABLE 77

The offspring given by the regular wild type daughters from table 74, culture 1079, when mated to bar males.

No.	Regular offspring					Exceptions		
	B′ ♀	w^ev ♂	+ ♂	w^e ♂	v ♂	+ ♀	B′ ♂	Percent
1182	89	29	25	11	11	4	4	4.6
1204	8	2	3	—	2	—	—	—
1205	26	12	3	2	3	3	4	13.2
1217	116	37	34	20	17	9	5	5.9 (w^e ♀ 2, v ♀ 2)
1222	6	5	3	2	1	—	—	—
1164	30	—	13	6	—	20	15	42.
1183	78	—	36	40	—	—	—	—
1203	91	—	38	42	—	—	—	—
1206	15	—	6	8	—	1	5	16.6
1221	97	—	47	32	—	7	6	6.9 (w^e ♀ 1)
1163	108	108 unclassified males				—	—	—
1185	85	110 unclassified males				—	—	—

Thirteen of the exceptional daughters from culture 1164, table 77, were outcrossed to bar males. The mean of the percentages of exceptional offspring was 5 percent, which is about normal, and there were no very high percentages (table 78).

TABLE 78

The offspring given by the wild type exceptional daughters from culture 1164, table 77, when mated to bar males.

No.	Regular offspring			Exceptions		
	B′ ♀	w^e ♂	+ ♂	+ ♀	B′ ♂	Percent
1238	148	52	53	3	3	2.3
1239	154	71	73	18	8	8.0
1240	188	90	84	8	7	4.0
1245	87	40	36	5	2	4.1
1246	146	83	59	3	3	2.0
1247	159	92	90	7	9	4.5
1248	100	47	52	8	6	6.6
1249	169	97	92	10	6	4.3
1250	154	85	85	6	7	3.9
1251	166	71	67	8	10	5.6
1252	152	68	77	11	9	6.3
1253	91	52	43	8	1	4.6
1289	182	88	84	18	11	7.6
Total	1896	936	895	113	82	5.0

Four of the regular bar daughters from culture 1164 were mated by white males. Only one produced exceptions, and the percentage was normal (table 79).

TABLE 79

The offspring given by four bar regular daughters from culture 1164, table 77, when mated to white males.

No.	Regular daughters				Regular sons				Exceptions	
	w-w^e	B′	w-w^{e}B′	+	w^e	B′	w^{e}B′	+	w ♂	Percent
1256	50	71	41	45	57	42	40	48	9	4.6
1257	21	19	11	10	26	16	10	10	—	—
1255	25	22	21	23	22	18	18	15	—	—
Total	46	41	32	33	48	34	28	25	—	—
1254	—	38	—	45	—	20	—	39	—	—

From the other unusually high culture (1202, table 76), four exceptional daughters were tested by mating to wild males. The percentages of exceptions were rather high (table 80).

TABLE 80

The offspring given by four white-eosin exceptional daughters from culture 1202, table 76, when outcrossed to wild males.

No.	Regular offspring		Exceptions		
	B′ ♀	Unclassified males	w-w^e ♀	+ ♂	Percent
1287	135	111	11	8	7.3
1288	135	137	3	13	5.6
1302	114	131	13	8	7.9
1336	130	113	8	13	8.
Total	514	492	35	42	7.1

Four other exceptional daughters tested by bar brothers gave normal percentages of exceptions (table 81).

These tests of the regular and exceptional daughters from the two unusually high cultures seem to show that the tendency to produce very high percentages is not due to anything which has happened to the X chromosome. If some sort of mutation in one or both of the X's was

TABLE 81

The offspring given by four white-eosin exceptional daughters from culture 1202, table 76, when mated to bar brothers.

No.	Regular offspring		Exceptions		
	B′ ♀	Unclassified males	w-w^e ♀	B′ ♂	Percent
1258	124	105	9	2	4.6
1285	174	176	11	8	4.9(yw ♀ 1)
1286	134	114	4	9	5.
1303	164	166	11	9	5.7
Total	596	561	34	28	5.1

responsible for this high non-disjunction, then all exceptional daughters, which receive both the X's of the mother, should also give high non-disjunction, but this was not the case.

Since secondary non-disjunction is caused by the presence of the Y chromosome, it seemed possible that the change in production of exceptions might be due to a change in the Y chromosome, that is, to a Y mutation. A high-producing female was assumed to be XXY′. Y′ would descend to all of the exceptional sons of such a female, and also to half of the regular daughters. All the exceptional sons of an XXY′ mother should be XY′ (see figure 6, p. 13). Since the effect of Y′ can only be detected in an XXY′ female, three of the exceptional bar sons (XY′) from culture 1202, table 76, were outcrossed to XXY exceptional daughters from table 44.

The XXY females to which the XY′ male is crossed should of course produce only the normal percentage of exceptions, as in fact they did (see cultures 1306, 1333, and 1304, table 45). All the exceptional daughters from these cultures should however be XXY′ and should give high non-disjunction. Two such daughters were tested by bar males and one gave very high non-disjunction (see culture 1417, table 45). The other culture, 1418, gave a rather low normal percentage.

The results are contradictory, but the partial success of the test encouraged further tests of the same nature. An attempt was made to secure a stock in which every Y, whether in females or in males, should be Y′. If culture 1417 was high because of the presence of Y′, then, as has been shown, the exceptional sons of this culture should also be XY′.

Since the father of culture 1417 was an ordinary bar male, all the exceptional daughters should be XXY and not XXY′. Matings between

these exceptional XXY daughters and XY′ sons should give normal percentages of exceptions, as was the case (see cultures 1612, 1613, 1618 and 1624, table 45).

The exceptional daughters from this last cross should be XXY′ and should give high non-disjunction. Three of them were mated to their *fathers* (which had been saved for this purpose), and since their Y's came from their fathers each of these cultures should give a line in which every Y is mutant. Also the percentages should be high from the XXY′ composition of the mother. Three such daughter by father matings were made and each gave a percentage above normal, but not unusually high (cultures 1703, 1714, 1715).

Evidently then, if there is a high line, the mode is in the neighborhood of 8 or 9 percent, with occasional very high cases. All the data secured in these tests will bear such an interpretation, but it cannot be considered proved until extensive tests of the percentages of exceptions given by the pure Y′ lines have been made.[10]

KEEPING STOCK

The method usually followed in keeping stock of non-disjunction is to breed from the exceptional females of any culture. These females have an extra Y chromosome and give exceptional daughters like themselves, and exceptional sons like whatever male was used in the outcross. In carrying on the stock in this fashion it is of course necessary that the females be virgin, and this involves the inconvenience of watching the stock very closely, as the exceptional females are rare at best. A method which does not require such continuous attention is to mate an exceptional female, say eosin-eyed, to several of her brothers having eosin eyes. This will give an eosin stock which can be transferred from generation to generation. But in the use of such a stock, special precautions have to be taken, for not all the females will give exceptions when outcrossed. The initial eosin female had an extra Y, so that half of her sons and daughters will have one also. Moreover half of the eosin brothers to which such females are mated have an extra Y, so that an additional supply of Y's come from them. Only about three-eighths of all the flies of a freshly made stock will escape having an extra Y, while about one-eighth will have two extra Y's. In further generations of this stock the percentage of flies which have extra chromosomes may decrease. In carrying on a stock by a *few* parent flies in each generation, any mating which chances to

[10] Recently such tests have been made and they show that the mean of the high line is about 20 percent of exceptions.

have less than the average richness of Y's can not recover in the next generation, so that any particular poor selection will be a permanent injury to the stock.

In using such a stock one must make several P_1 matings in order to insure getting one in which the female carries an extra Y. As soon as such pairs have produced offspring one can select a culture which has given exceptions and discard the others. Of twenty-six such matings made from fresh stocks, only six failed to give exceptions (table 82).

TABLE 82

The three kinds of results given by eosin females of fresh stocks of non-disjunction when tested by wild males.

No.	Regular offspring		Exceptions		Percent of exceptions
	+ ♀	w^e ♂	w^e ♀	+ ♂	
62n	130	122	2	1	1.2
63n	69	60	6	5	7.9
64n	70	84	1	—	.6
66n	43	24	3	4	9.5
68n	64	64	4	5	6.6
69n	94	91	7	10	8.4
70n	72	52	6	16	15.1
71n	65	48	4	3	5.8
88n	59	62	1	4	4.
89n	45	59	—	2	1.9
90n	50	52	1	2	2.9
91n	24	27	—	1	1.9
92n	83	76	3	2	3.
93n	81	64	6	—	4.
95n	50	40	1	2	3.2
96n	37	42	1	—	1.3
140n	82	80	3	4	4.1
141n	33	30	2	—	3.1
142n	53	50	1	—	1.
145n	22	32	—	1	1.8
Total	1226	1159	52	62	—
61n	49	56	—	—	—
65n	121	119	—	—	—
67n	75	79	—	—	—
94n	79	77	—	—	—
97n	44	35	—	—	—
128n	110	90	—	—	—
Total	478	456	—	—	—

Tests made with a stock which had been maintained by transference in this manner through five months showed little deterioration, since four out of six females tested gave exceptions (table 83).

TABLE 83

The offspring given by six eosin females, from a stock transferred through five months, mated to bar males.

No.	Regular offspring		Exceptions		
	B′ ♀	w^e ♂	w^e ♀	B′ ♂	Percent
119n	50	48	—	1	1.
121n	54	54	—	1	1.
122n	68	71	7	8	9.7
124n	45	63	1	1	1.8
Total	217	236	8	11	—
120n	82	82	—	—	—
123n	41	48	—	—	—
Total	123	130	—	—	—

However, from another stock which had been kept about five months only four females out of the twenty-three tested gave exceptions (table 84).

TABLE 84

The offspring given by eosin females, from a stock transferred through eight generations, when mated to vermilion males.

No.	Regular offspring		Exceptions		Percent
	+ ♀	w^e ♂	w^e ♀	v ♂	
295	35	40	—	1	1.3
319	54	38	—	1	1.1
321	17	19	1	—	2.3
322	10	14	—	1	4.1
Total	116	111	1	3	—
296	55	54	—	—	—
297	38	14	—	—	—
298	87	61	—	—	—
299	35	37	—	—	—
307	35	21	—	—	—
308	64	31	—	—	—
309	53	53	—	—	—
310	35	27	—	—	—
311	31	29	—	—	—
312	31	26	—	—	—
313	29	17	—	—	—
314	11	10	—	—	—
315	29	23	—	—	—
316	31	23	—	—	—
317	52	21	—	—	—
318	35	24	—	—	—
320	43	28	—	—	—
323	61	50	—	—	—
324	52	47	—	—	—
330	34	30	—	—	—
331	35	31	—	—	—
332	38	33	—	—	—
Total	914	690	—	—	—

It will be noticed that not more than one exception appeared in any of the cultures of this table. It is very possible that some of these may be primary exceptions, in view of the frequency with which primary non-disjunction must be supposed to occur. Moreover, all three of the regular daughters of culture 321 which were tested failed to give exceptions, as would be the case if the exception in 321 were primary (table 85).

TABLE 85

The offspring given by three wild type regular daughters from culture 321, table 84, when mated to bar males.

No.	Regular offspring		Exceptions	
	B′ ♀	Unclassified males	+ ♀	B′ ♂
389	105	94	—	—
390	102	123	—	—
391	78	66	—	—
Total	285	283	—	—

For the most part there has been no need for special stock of non-disjunction, since the experiments have continually furnished material for fresh work. Those few cultures which have had little purpose aside from keeping stock are summarized in table 86. The pedigree gives the relation of each culture to the whole fabric. Culture 339 was intended as part of an experiment with certain eye-colors, but since it gave secondary exceptions of a convenient kind a new line of non-disjunction was started and the old line was terminated.

TABLE 86

Miscellaneous cultures.

Parents	No.	Regular daughters	Regular sons	Exceptions	Percent of exceptions
w^e ♀ × w ♂		w-w^e	w^e	w^e ♀ w ♂	
	43n	82	88	8 12	10.5
w^e ♀ × wB′ ♂		w-w^eB′	w^e	w^e ♀ wB′ ♂	
	42n	66	88	5 2	4.4
+ ♀ × wB′ ♂		w-w^eB′ B′	w^e +	+ ♀ wB′ ♂	
	58n	18 25	25 32	1 2	2.9
	60n	19 39	32 26	2 2	3.3
		37 64	57 58	3 4	
w^e ♀ × B′ ♂		B′	w^e	w^e ♀ B′ ♂	
	152n	40	24	2 2	5.9
	153n	37	38	2 5	8.5
		77	62	4 7	
v ♀ × + ♂		+	v	v ♀ + ♂	
	339	77	73	10 10	11.8
v ♀ × B′ ♂		B′	v	v ♀ B′ ♂	
	419	190	160	3 4	2.0
	420	164	169	3 1	1.2
	421	189	159	2 —	0.6
	429	205	142	2 3	1.4
	430	106	97	2 —	1.0
		854	727	12 8	
+ ♀ × wB′ ♂		w-w^eB′ B′	w^e v w^ev +	+ ♀ wB′ ♂	
	649	60 63	46 38 20 16	3 2	2.0

MUTATIONS

The cultures reported in this paper have given rise to over a dozen mutations, and these may be briefly described.

Cream a (July 15, 1915). It was noticed that some of the eosin males of culture 43n (table 86) were considerably lighter than normal and were a pale yellow or "cream" color. A "cream" male was outcrossed to a wild female and gave wild type sons and daughters as expected if the cause of the dilution were recessive. An F_1 pair produced

a surprising F_2 result, which differed from the result of the simple F_2 from an eosin male by wild female only in that a quarter of the flies which were eosin were diluted to cream. None of the not-eosin flies showed a trace of dilution. The character "cream" is then a double recessive, the product of the action of a recessive autosomal gene ("cream," by extension) added to the effect of the sex-linked gene eosin. However, the single recessive, cream, is indistinguishable from red, that is, by itself it produces no visible effect. Cream *a* was the first of a class of mutations which are specific diluters of eosin, that is, which require the presence of eosin before they can develop any visible effect. These specific modifiers are analogous to the modifiers which extend or restrict the area of the white pigment of the hooded rat, and which produce no visible effect unless the white-producing gene is present as a base.

Dark and *whiting* (Sept. 23, 1913 and Nov. 21, 1913). It was noticed that in the sister cultures 100n and 101n (table 16), there were present eosin males which were abnormally dark in color. In the next generation more dark males appeared, and some of the white-eosin females were practically as dark as pure eosin. In subsequent generations this dark modification appeared in a manner and in such proportions as to suggest that it was a case converse to cream *a*, that is, that there was present a recessive gene which is a specific darkener of eosin, and which does not modify the color of those flies which are not eosin.

One pair of "dark" eosin flies gave about a quarter of the offspring pure white in eye-color (Nov. 21, 1913). This was an astonishing result, since the sex-linked white could not appear among the daughters of such a culture except by the rare equational non-disjunction. Other features of the cross were likewise impossible on the assumption that the colorless eye was the sex-linked white. A series of tests showed that this white color was in fact not the sex-linked white which had been running through the experiments up to this point, but was a new and complex color due to a specific diluter of eosin, that the white was a double recessive, eosin "whiting." It is remarkable that a gene which has so profound an effect upon eosin (depriving it of all trace of color in both males and females) should by itself produce no visible effect; the stock of whiting is indistinguishable from a wild stock, and the eosin whiting is indistinguishable from white. How curiously specific is the dilution effect of whiting, is illustrated by the fact that whiting does not affect cherry, an allelomorph of eosin so similar to eosin that cherry and eosin females are practically indistinguishable.

Cream b (March 10, 1914). In culture 82 (table 41) a single eosin male somewhat lighter in color than the others was observed. This dilution was found to be due to an autosomal diluter like cream *a* though not as marked in its effects.

Three other specific diluters of eosin have come up in my experiments. A remarkably close imitation of such a multiple factor case as that of CASTLE's hooded rats could be concocted with the chief gene eosin for reduced color, and these six diluters which by themselves produce no effect, but which carry the color of eosin through every dilution stage from the dark yellowish pink of the eosin female to a pure white.

Lethal 4 (March 13, 1914). The same culture, 82 (table 41), which gave rise to cream *b* gave only half as many sons as daughters. The cause of this absence of sons was found to be a sex-linked lethal gene whose locus in the X chromosome is at approximately 49.

Lethal 6 (April 9, 1914). The cream *b* male of culture 82 (table 41) was outcrossed to a wild female, and a pair of F_1 flies gave only half as many sons as daughters. These sons were all eosin, so that the death of the wild type sons must have been due to a lethal (lethal *6*) which was carried by the X from the wild grandmother. This lethal is interesting since it has been found to lie to the left of yellow at a position —.04. This is the closest "partial" linkage recorded, there being only one crossover between lethal *6* and yellow in 2500 flies.

Spoon (December 12, 1914). In culture 898 (table 37 (*B*)) a male was found which had a thin-textured wing, curved like the bowl of a spoon and having an extra cross vein. This mutation proved to be a sex-linked recessive which lies to the left of eosin and close to yellow. However, only rarely do spoon flies hatch, so that the character has to be handled like a lethal, with the exception that the occasional spoon male can be used in mating—an advantage lacking in the case of total lethals. This mutation is a sort of connecting link between those mutations, such as rudimentary, which are poorly viable under adverse conditions, and total lethals which never hatch under any condition. One class of lethals can be regarded as an extension of this inviability effect to the point at which the mutant individuals can no longer hatch.

Lethal 7 (January 1, 1915). Another category of lethals is illustrated by lethal *7* which appeared in culture 1072 (table 61). This lethal, which also lies to the left of eosin, causes the death of the individual at the mature larval stage. Those larvae which are about to die can be separated from those which are to live, because the morescent larvae,

when half mature, leave the food and wander about on the surface of the culture bottle. Furthermore, while these larvae are still young one or more intense black specks appear in their body-cavities. As the larvae become older this character, which is absent from normal flies, becomes more conspicuous, so that one can easily pick out those cultures in which the mother was heterozygous for lethal 7 by the numbers of black-spotted larvae wandering about or dead upon the walls of the bottle. Lethal 7 is then a larval character of such virulence as to cause a change in the instincts of the individual and finally to cause its death.

Deficiency (September 25, 1914). Still another and the most significant category of lethals was found in the appearance in culture 546 (table 9) of a white-eosin daughter from a mother heterozygous for eosin and a father which was white but also bar. *This daughter received the white from the father but did not receive his bar.* Since both white and bar are carried by the X chromosome, either bar remutated to normal or something happened to the region of the X in which bar was situated. Tests showed that the latter explanation was correct, that a small section of the X in the bar region had become genetically non-existent! This X, at the same time that it lost the gene for bar, lost the normal allelomorph for forked, which is about half a unit from bar. Females having one normal X and one deficient X, outcrossed to forked males, produced daughters half of which were forked, and this in spite of the fact that forked is a strict recessive. These forked daughters have forked in the paternal X and in the maternal (the deficient X) no allelomorph of forked whatever. This deficient region is known to extend from forked to bar and to fail to extend to rudimentary (rudimentary is 1.4 units to the left of forked) on the one hand and to fused on the other (fused is 2.3 units beyond bar). The existence of normal genes and their allelomorphs between the deficient region and the end of the X proves that the end is not gone but that the change is an internal one which affects a specific region of the hereditary material. A female having one deficient X shows no crossing over in the region between forked and bar. The section of the X chromosome from forked to bar exhibits properties like those of the Y chromosome; perhaps the lack of genetic material in the Y has been brought about through the same process which occurred in the X of the white bar male.

A female having one deficient X gives only half as many sons as daughters, that is, a male is unable to live unless he has a whole X.

It should be noticed that this first case in which a true "loss" of

genetic material is known to occur is unaccompanied by any visible mutative change; the female having a section of the essential genetic material gone from one X is entirely normal in appearance. This is of great significance since the loss involves the region in which the dominant bar is situated. If the dominance of bar were due to the loss of an inhibitor then this female should have been bar, which she was not. The expedient of explaining a dominant as the loss of an inhibitor is useless in this case and of extremely questionable value in most other cases.

Of considerable theoretical importance is the fact that an individual having one deficient chromosome is a *female,* normal in appearance and function. Therefore it is not essential for the production of a female that two whole X's be present, that is, sex production is a function of some particular part of the X rather than of the X as a whole; further, the sex differentiators are situated in some region of the chromosome *other than the region from forked to bar.* It may be long before we know in what region the sex differentiators are, but meanwhile it is some satisfaction to know where they are not.

Short (July 20, 1914). In culture 310 (table 84) all the males that were eosin had wings of about half or two-thirds normal length and of conspicuous broadness. This mutation proved to be sex-linked and to be located between yellow and white.

Bifid (July, 1914). In culture 323 (table 84) the sex-linked mutation bifid reappeared.

Rudimentary (July, 1914). In culture 330 (table 84) the sex-linked mutation rudimentary reappeared. Both bifid and rudimentary were checked by the presence of eosin, and by the fact that they occurred at Cold Spring Harbor where there were no stocks of these mutations.

Confluent (September 23, 1914). In culture 550 (table 9) appeared a single male with the veins of the wing thickened and knotted and confluent with the marginal vein. This mutation was a second-chromosome dominant, which was probably lethal when homozygous (yellow mouse case). The interesting feature of this mutation was that C. W. METZ and B. S. METZ (1915) found in another species of Drosophila a mutation which corresponded with this mutation in all points, both as to its somatic appearance and genetic behavior.

Garnet (February 19, 1915). In culture 1347 (table 34) one of the sable sons had an eye-color which was practically indistinguishable from

purple (purple is a second-chromosome mutation). The new color "garnet" proved to be sex-linked and to be located at about 44.4.

III

OTHER EXCEPTIONS TO SEX-LINKED INHERITANCE, AND VARIATIONS IN THE DISTRIBUTION OF CHROMOSOMES

In several other forms exceptions occur which seem to be of the same type as those found in Drosophila,—namely, matroclinous daughters and patroclinous sons. Cytological work has shown that in many forms the chromosomes are subject to variations in distribution and constitution. While it is not probable that all these variations can be fully explained by non-disjunction, yet it may be profitable to point out how far they may be accounted for on this theory.

Abraxas

One of the most extensive cases to which the explanation of non-disjunction seems to apply is that of the exceptions to sex-linked inheritance which DONCASTER has found in Abraxas. The wild form of Abraxas is *grossulariata*. A rare variety, *lacticolor*, characterized by smaller and paler markings, behaves as a recessive sex-linked character, as is shown by the cross of *lacticolor* male by *grossulariata* female, which gives *lacticolor* daughters and *grossulariata* sons. This "criss-cross" inheritance, which is characteristic of sex-linkage, is here of a type which is the converse of that found in Drosophila, and is explained by assuming that in Abraxas the female is heterozygous as regards the sex-differentiator and sex-linked characters. For convenience in referring to cases of the Abraxas type we may call the sex chromosome present in the homozygous sex, which in this sense corresponds to the X of Drosophila, a Z chromosome, while the chromosome corresponding in this sense to the Y of Drosophila may be called a W chromosome. The formulae are then:

Abraxas type $\begin{matrix} ♂ = ZZ \\ ♀ = ZW \end{matrix}$ corresponding to $\begin{matrix} XX = ♀ \\ XY = ♂ \end{matrix}$ Drosophila type.

DONCASTER found in Abraxas that both the female and the male have 56 chromosomes.

Normally in Abraxas the sex-ratio is approximately 1♀ : 1♂, but in one exceptional line the equality of sexes is not the rule. In this strain

DONCASTER (1913, 1914 a, b) found many females which gave only daughters and not a single son. Other females of this line gave many daughters but also a few sons, while still others gave practically a normal 1 : 1 ratio.

When DONCASTER examined this line cytologically, he found that although the males were normal, with 56 chromosomes, the females were aberrant and had only 55 chromosomes. Even those females which gave 1 : 1 ratios had only 55 chromosomes. In the maturation of the eggs of such a 55 chromosome female, the odd chromosome went to one pole, so that one polar plate had 27 and the other 28 chromosomes. DONCASTER found further that the odd chromosome went most often to the polar body, leaving a majority of the eggs after maturation with 27 chromosomes.[11] After fertilization, the many eggs which eliminate the odd chromosome become individuals with 55 chromosomes, that is, females, while the few eggs which retain it become 56-chromosome individuals, that is, males. The preponderance of females in the strain is thus explained. Such females, having only 55 chromosomes, would be of the type ZO. In females of normal strains there is a W chromosome present, but since this W chromosome may be absent without effect upon the sex of the individual, it must be regarded as functionless in determining sex, and in this sense corresponds to the Y of Drosophila. This evidence proves that there is present in Abraxas that cytological basis which the evidence from sex-linkage demands, namely, a condition the converse of that known in other groups of insects.

The loss of a chromosome from this strain with 55 chromosomes instead of 56 can be readily accounted for by primary non-disjunction. Suppose that in the male the two Z chromosomes should both pass at the reduction division into one cell, leaving the other cell with no Z. The sperm produced from the latter cell, fertilizing a Z egg, would give rise to a ZO female. The same result could be reached if both Z and W should pass out into the polar body of the egg and such an egg be fertilized by ordinary Z sperm, thereby producing a ZO female. The strain once established would continue automatically to give ZO females with 55 chromosomes and ZZ males with 56 chromosomes.

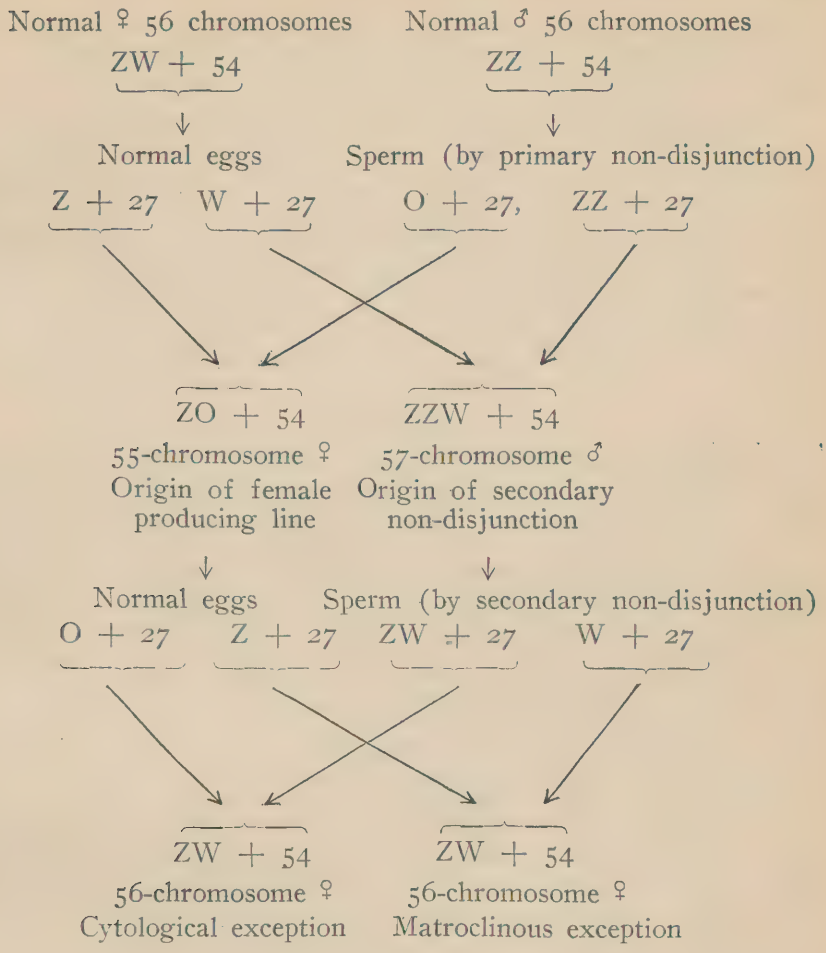
If non-disjunction is the explanation of the origin of the 55-chromosome female line, then we may expect to find other evidences of non-

[11] Recently DONCASTER has published a short note (Nature, June 10, 1915) in which he states that a more extensive examination of the reduction divisions has failed to show that the 27 chromosome eggs are more numerous than the 28. This contradiction in the evidence detracts much from the value of the case as it now stands.

disjunction in Abraxas. At various times DONCASTER has found genetic exceptions of the same character as are found in Drosophila, and in the case of some of his exceptions there can be small chance of error.

There is also cytological evidence derived from the examination of a certain female that occurred in one of the same broods that gave exceptions to sex-linked inheritance. This female had 56 chromosomes although she was from a strain of which the females normally have only 55 chromosomes. The additional chromosome in this female can be accounted for on the supposition that her father had a supernumerary W chromosome. Such a supernumerary could arise in a male through the fertilization of a W egg by a sperm which receives two Z chromosomes by primary non-disjunction. Such a ZZW male would produce some sperm having both Z and W. A ZW sperm fertilizing an egg without a Z would produce a ZW female with 56 chromosomes, such as DONCASTER found. In the same brood in which DONCASTER found this 56-chromosome female, he found two matroclinous daughters. These also can be readily accounted for in the following way. In the spermatogenesis of the ZZW father there would be formed some sperm having only W (corresponding to the Y eggs of Drosophila.) This W sperm fertilizing a Z egg of the ZO mother would give a ZW daughter which would have 56 chromosomes. But in this case the daughter would have received her Z chromosome from her mother, so that she should show the sex-linked character of the mother, that is, she should be a matroclinous exception like the two DONCASTER found in the brood.

That non-disjunction occurs in the wild Abraxas is indicated by the discovery of a wild female with 55 chromosomes. This 55-chromosome female with the formula ZO is the converse of the ZZW male required in the explanation above. The following diagram illustrates the probable origin of the ZO female line and of the ZZW males, and also of the exceptions observed.



If non-disjunction is the correct explanation of the case just reviewed, then we may hope to obtain females and males with 57 chromosomes. When exceptions to sex-linked inheritance occur, then half the sons and daughters in the brood should have a supernumerary, if the exceptions are due to secondary non-disjunction. If the exceptions are due to primary non-disjunction,—a much rarer phenomenon,—then only an occasional individual with the supernumerary should be found. The supernumerary would be only half as common in a cross in which the mother was herself without a W. The cross most favorable for observing exceptions and for obtaining supernumeraries would be that of a *lacticolor* male by a wild *grossulariata* female. If an exceptional son should appear in this cross, he should give some exceptional sons like

himself and some matroclinous daughters, since he would be of the composition ZZW. Furthermore, half of his sons and daughters should have 57 chromosomes and half 56.

The explanation which DONCASTER has suggested for some of these exceptions depends upon the assumption that the Z chromosome has divided into two chromosomes, one of which bears the locus for *lacticolor* and the other of which bears the sex-differentiator. As far as the evidence enables us to decide, this hypothesis explains some features of the case as well as does non-disjunction. The notable exception which it does not seem to explain is the production of the 55-chromosome line.

Paratettix

In Paratettix, NABOURS (1914) has reported a case of genetic exception for which two alternative explanations have been offered (DEXTER 1914). NABOURS collected nine distinct true-breeding wild forms, of which eight form a system of multiple allelomorphs or a system of practically complete linkage, while the form *melanothorax* (G) is independent of the others in inheritance. In "The mechanism of Mendelian heredity" reasons have been given for considering multiple allelomorphism the more probable explanation. This material is exceptionally favorable in one respect—that the color-patterns studied are superimposed in the hybrids so that the zygotic constitution of any individual can be determined by simple inspection.

In one of NABOURS's experiments, a BI female mated to a CE male, gave, as expected, equal numbers of the four classes BC, BE, CI, and EI, but gave in addition an exceptional individual of the constitution BIE.

If BI and E are members of a multiple allelomorph system, which is the most probable case, then in the egg which gave rise to this BIE individual, non-disjunction must have occurred whereby the B and I bearing chromosomes both remained in the egg. This BI egg fertilized by an E sperm from the CE father, would give the BIE individual. Such an individual should have three homologous chromosomes, and a total of one more than the number characteristic of the species. Genetically, also, the results should be very easy to test, for secondary non-disjunction should occur, wherefore half the offspring should be further triple forms of various constitutions. B and I should freely separate, for it is improbable that there would be preferential synapsis between these chromosomes which are not dissimilar, as they are in Drosophila in the case of XXY and XYY. On the other hand, if the case is one of linkage,

the BIE individual is explained as a crossover, and it should have no extra chromosome. In subsequent generations B and I should not freely separate but should remain coupled as strongly as they were repulsed before. It is to be hoped that another triple-charactered individual will be found, for genetic and cytological tests of it would be of exceptional interest. The study of non-disjunction of *autosomes* is extremely difficult in ordinary forms where the constitution of each individual must be found by laborious breeding tests, but in case the three chromosomes of the non-disjunctional individual each contain a different allelomorph of a multiple allelomorph series, and this triple form is distinguishable, then such a study should be easy.

Oenothera lata and Oe. semilata

A case of autosomal non-disjunction which has been thoroughly studied is that of *Oenothera lata* and *Oe. semilata* (LUTZ 1912, GATES and THOMAS 1914). The cytological and breeding work have shown that these forms are due to the possession of an extra chromosome, that is, one of the autosomes is triploid. *Lata* and *semilata* occasionally arise directly from *Oe. Lamarckiana,* and the explanation is found in the fact that occasionally in the gametogenesis of *Lamarckiana* a pair of synapsed chromosomes fail to disjoin and pass to the same pole (primary non-disjunction). The fact that the possession of three autosomes of one kind makes the individual visibly different from *Lamarckiana* is of great convenience in studying non-disjunction, for the offspring which possess a triploid chromosome do not have to be tested, as in the case of Drosophila, but can be readily distinguished as *lata* or *semilata.* Secondary non-disjunction occurs in the *lata;* at reduction the free chromosome passes to one pole or the other so that half the gametes are *aa* and half are *a.* This is not strictly true, for very often the free autosome lags upon the spindle and so fails to be included in either nucleus. A *lata* individual thus produces less than the expected percent of *aa* gametes. This is strictly paralleled by the result of crossing *lata* (*aaa*) to *Lamarckiana* (*aa*), for where this cross is expected to give half *lata* and half *Lamarckiana,* it rarely gives as many as half the plants *lata.*

Pigeons

Exceptions to the inheritance of the blond and the dark types of pigeons have been explained as partial sex-linkage (BRIDGES 1913 a), but non-disjunction offers an alternative explanation which seems more plausible.

Canaries

Exceptions to sex-linkage in the inheritance of pink versus black eye-colors have been reported (DURHAM and MARRYATT 1908). These exceptions are explainable by non-disjunction or by partial sex-linkage.

Fowls

BATESON and PUNNETT (1911) reported several exceptions in the inheritance of pigmentation of the silky fowl, which may be due to non-disjunction.

Aglia tau and A. lugens

STURTEVANT (1912) interpreted as partial sex-linkage the ratios observed by STANDFUSS (1896) in breeding *Aglia tau* and its variety *lugens*. This explanation seems to fit the data empirically and it is difficult to explain the results as due to non-disjunction. More recent data by STANDFUSS (1910) throw some doubt on this case. Similar results have been obtained occasionally in Drosophila, but have never been capable of repetition and are probably due to irregularities of viability caused by unfavorable culture-conditions. The hypothesis of partial sex-linkage has met a serious difficulty in the fact that in Drosophila and in the silk worm moth there is no crossing over in the heterozygous sex.

Cats

Apparent exceptions to sex-linkage in cats have been explained satisfactorily by WHITING (1915) without recourse to partial sex-linkage or to non-disjunction. WHITING offers evidence which shows that there are extension and restriction factors for yellow and black so that the apparent exceptions are simply modified classes which are expected.

Metapodius

WILSON (1907, 1909, 1910) found that in Metapodius the number of Y chromosomes varied from zero to six, and he offered the explanation that the origin of the variation was in an aberrant reduction division in which both sex chromosomes entered the same gamete. WILSON actually observed three reduction divisions in which X followed Y to one pole. This constitutes primary non-disjunction. The subsequent piling up of Y's was due to secondary non-disjunction. WILSON (1910) explained the mmm individual of Metapodius in the same fashion, by assuming the formation of an mm gamete.

Banasa

In *Banasa calva* WILSON (1907) found that the Y chromosome may be present or absent.

Diabrotica

STEVENS (1908 b, 1912 a) described in *Diabrotica soror* and *D. vittata* a variation in the number of Y's from one, the normal number, to five supernumeraries, or six Y's in all.

Ceuthophilus

A like variation was described by STEVENS (1912 b) in Ceuthophilus, where the number of supernumerary Y's was three.

These cases in Metapodius, Banasa, Diabrotica, and Ceuthophilus are cytologically of the same kind as that in Drosophila.

Ascaris

Miss BORING (1909) found in Ascaris a small extra chromosome which was interpreted as the X, which ordinarily is attached to the end of an autosome. S. FROLOWA (1912) found cases in Ascaris in which two of these X's seemed to be attached to the same autosome. These two X's would be carried into the same gamete and should give results comparable to non-disjunction.

IV

SUMMARY AND CONCLUSIONS

Evidence has been presented which proves that the occasional (1 in 1700) matroclinous daughter or patroclinous son produced by females known to be XX in composition is due to primary non-disjunction, that is, the X's fail to disjoin and are both included in the egg or both extruded to the polar cell.

The fertilization of the zero egg by an X sperm of a normal male results in a patroclinous XO son. He is entirely unaltered in somatic appearance, both as to sex-linked characters and as to sexual characters, but he is absolutely sterile. This difference between XO and XY males proves that the Y has some normal function in Drosophila.

The fertilization of an XX egg by a Y sperm of a normal male gives rise to a matroclinous daughter of the constitution XXY. The consti-

tution of a matroclinous female as XXY has been proved by direct cytological examination and by conclusive genetic tests.

Matroclinous females always produce further exceptions which we may call secondary, to the extent of 4.3 percent. The cause of this production is the fact that the presence of the extra Y forces both X's to enter the same cell in a certain percent of reductions.

In an XXY female the sex chromosomes do not synapse as a triad, but two synapse, leaving the third unsynapsed. Synapses are not at random, but are highly preferential; in 16.5 percent of cases Y synapses with one or the other X (heterosynapsis) and the remaining X is unsynapsed; in 83.5 percent of cases synapsis is between X and X (homosynapsis) and the Y is unsynapsed.

At the reduction division the two synapsed chromosomes disjoin and pass to opposite poles. The free chromosome goes with one or the other at random.

Reductions are not preferential; the polar spindle delivers two chromosomes to the polar cell as often as to the egg.

After XX synapsis the amount of crossing over is slightly increased (13.5 percent) in some manner by the presence of the extra Y.

After XY synapsis there is no crossing over—either between the X and Y or between the synapsed X and the free X.

After XY synapses the eggs are XX and Y, and X and XY. These four classes of eggs are in equal numbers and are non-crossovers.

The XX eggs by Y sperm give matroclinous daughters which are exact reproductions of the mother in all respects.

The Y eggs by X sperm give patroclinous sons which can give non-disjunctional effects neither in F_1 nor in F_2.

The X and XY eggs from XY synapses are indistinguishable from the non-crossover classes of the X and XY eggs which are from XX synapses. As a result the linkage values must be corrected.

The XY egg by X sperm gives an XXY regular daughter which nevertheless gives 4.3 percent of secondary exceptions by virtue of the extra Y.

YO, YY, and XXX zygotes are unable to live.

The XY egg by Y sperm gives XYY males. These males produce no exceptions in F_1 but produce XY sperm which, fertilizing X eggs, give rise to XXY daughters, and these produce secondary exceptions.

Synapses in an XYY male are probably at random.

The source of chromosomes, whether maternal or paternal, is without effect upon their subsequent behavior at synapsis and reduction.

The predominant type of non-disjunction has been shown to be pre-

ceded by XY synapsis and to take place at the reduction division. A rare type of non-disjunction takes place at an equational division. Equational non-disjunction is apparently always preceded by XX synapsis and crossing over. Equational non-disjunction offers the possibility of determining whether crossing over in Drosophila takes place by the chiasmatype (four strand stage) method or at a two strand stage.

Somatic non-disjunction explains the occurrence of gynandromorphs and mosaics in Drosophila.

Unusually high percentages of exceptions occur and are irregularly inherited. It is suggested that the cause of the high non-disjunction is a mutation in the Y chromosome.

The occurrence of non-disjunction in Abraxas is shown both by cytological and by breeding tests. Various other forms, namely, canaries, fowls, pigeons, and the moth, *Aglia tau*, show exceptions to sex-linkage which may be explained as due to non-disjunction.

In *Oenothera lata*, autosomal non-disjunction has been studied. A single tri-allelomorphic individual in Paratettix may be due to autosomal non-disjunction.

The occurrence of supernumerary Y chromosomes and of triploid or multiple chromosomes in various forms can likewise be explained as the result of non-disjunction.

The genetic and cytological evidence in the case of non-disjunction leaves no escape from the conclusion that the X chromosomes are the carriers of the genes for the sex-linked characters. The distribution of sex-linked genes (as tested by experimental breeding methods) has been demonstrated to be identical, through all the details of a unique process, with the distribution of the X chromosomes (as tested by direct cytological examination). The argument that the cell as a whole possesses the tendency to develop certain characters is completely nullified by the fact that in these cases the cells that produce exceptions are of exactly the same parentage as those which do not produce exceptions, the only difference being the parentage of a particular chromosome, the X. Those eggs which have lost nothing but the X chromosome have completely lost therewith the ability to produce any of the maternal sex-linked characters, and with the introduction of an X from the father these eggs have developed all of the sex-linked characters of the father. Conversely, those eggs which have retained both X's of the mother and have received no X from the father show all of the sex-linked characters of the mother and none from the father. The breach which GREGORY found in his case of the tetraploid Primula, namely, that the doubling of

the genes is only an expression of the doubleness of the *cell-as-a-whole,* becomes in this case the strongest bulwark; for here the cell as a whole remains constant and the issue is restricted to *particular* chromosomes and a *particular* class of genes.

Experimental proof is given that particular chromosomes, the X chromosomes, are the differentiators of sex; the X chromosome constitution of an individual is the cause of the development by that individual of a particular sex, and is not the result of sex already determined by some other agent. The sex is not determined in the egg or the sperm as such, but is determined at the moment of fertilization; for the X sperm of a male gives rise to a female when it fertilizes an egg containing an X, but to a male if it fertilizes an egg containing a Y or no sex chromosome at all. Likewise the Y sperm of a male gives rise to a female when fertilizing an XX egg and to a male when fertilizing an X egg. These facts in connection with the fact that an X egg of a female produces a male if fertilized by an X sperm prove that the segregation of the X chromosomes is the segregation of the sex-differentiators. The presence of two X chromosomes determines that an individual shall be a female, the presence of one X that the individual shall be a male. The origin of these chromosomes whether maternal or paternal is without significance in the production of sex.

The Y chromosome is without effect upon the sex or the characters of the individual, for males may have one Y, two Y's, or may lack Y entirely (males lacking Y are sterile); and females may have one or two supernumerary Y's with no change in appearance in any case.

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